

# Human CD20 Transgene expression in mouse B220<sup>+</sup> cell

Inventor: CHAN et al.  
Docket No.: 11669.0150USW1  
Title: TRANSGENIC MICE EXPRESSING HUMAN CD20 AND/OR CD16  
Attorney Name: Katherine M. Kowalchuk  
Phone No.: 612.371.5311  
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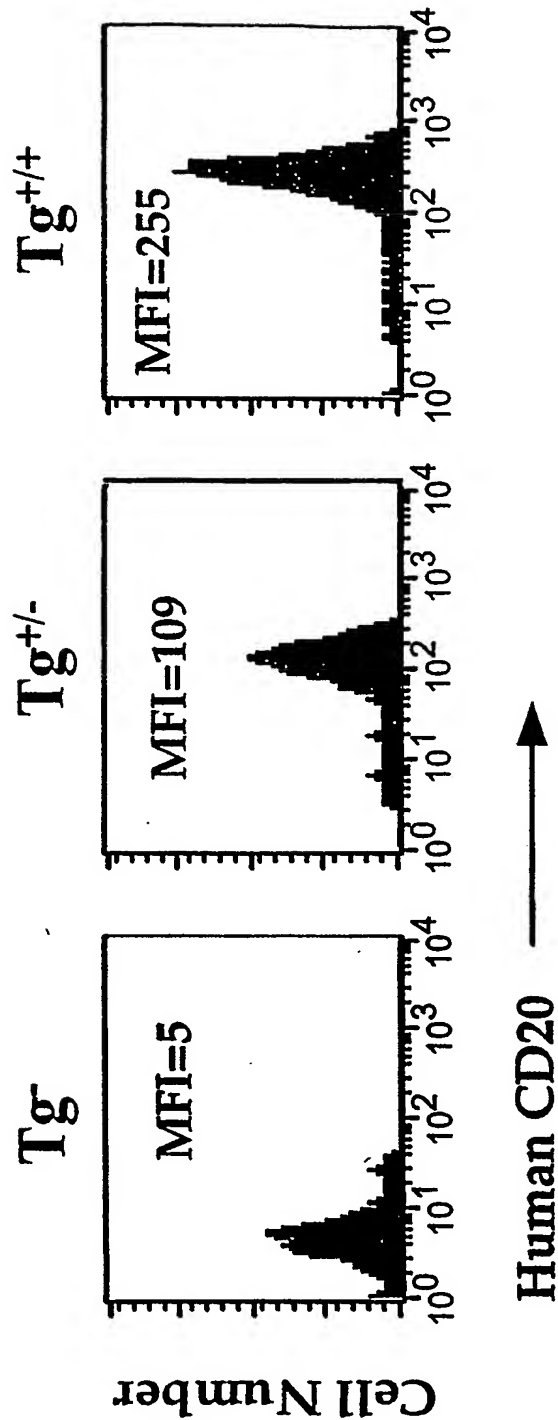


Figure 1

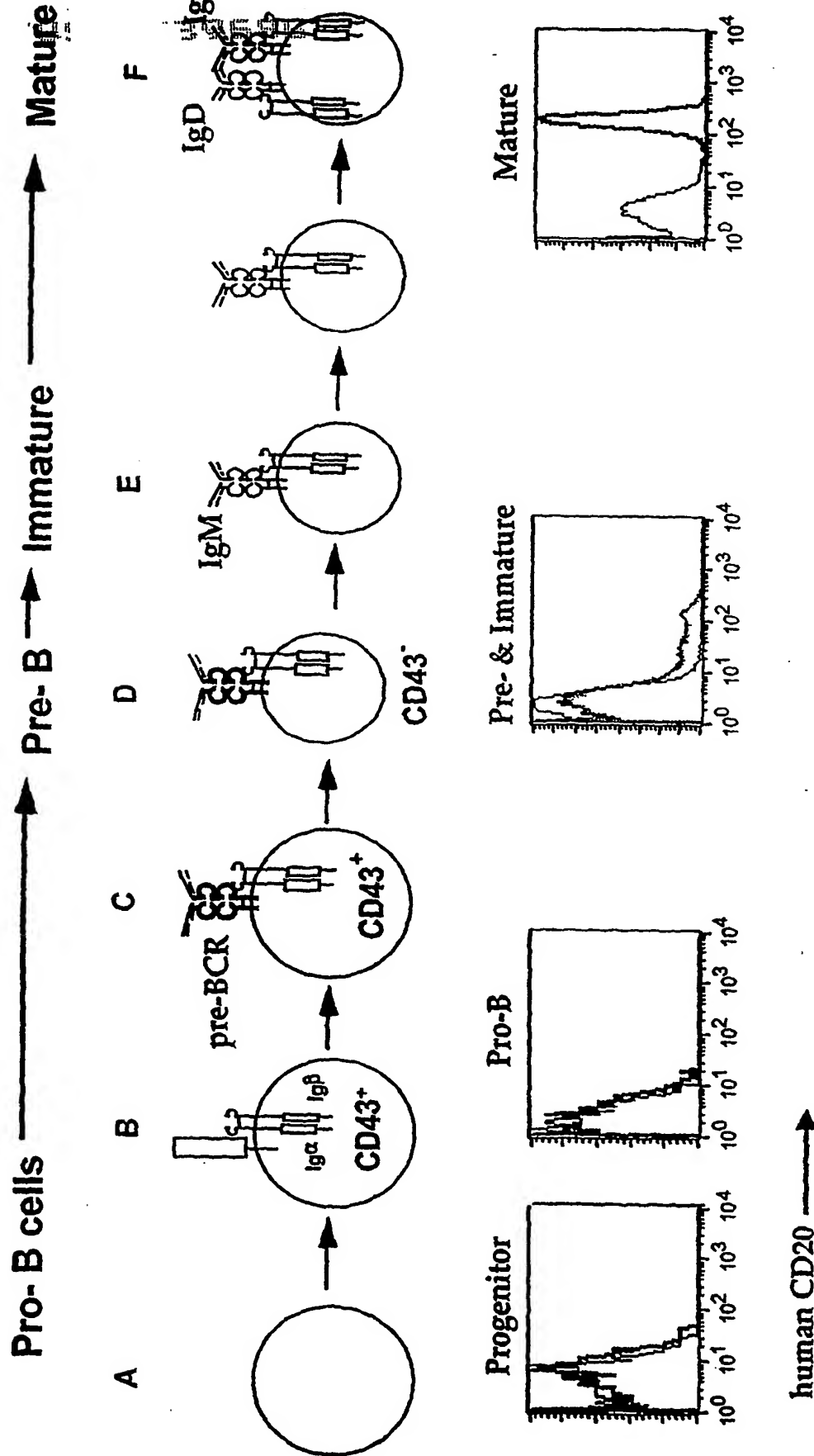


Figure 2

# Expression of human CD20 in Tg<sup>+</sup> mouse bone marrow

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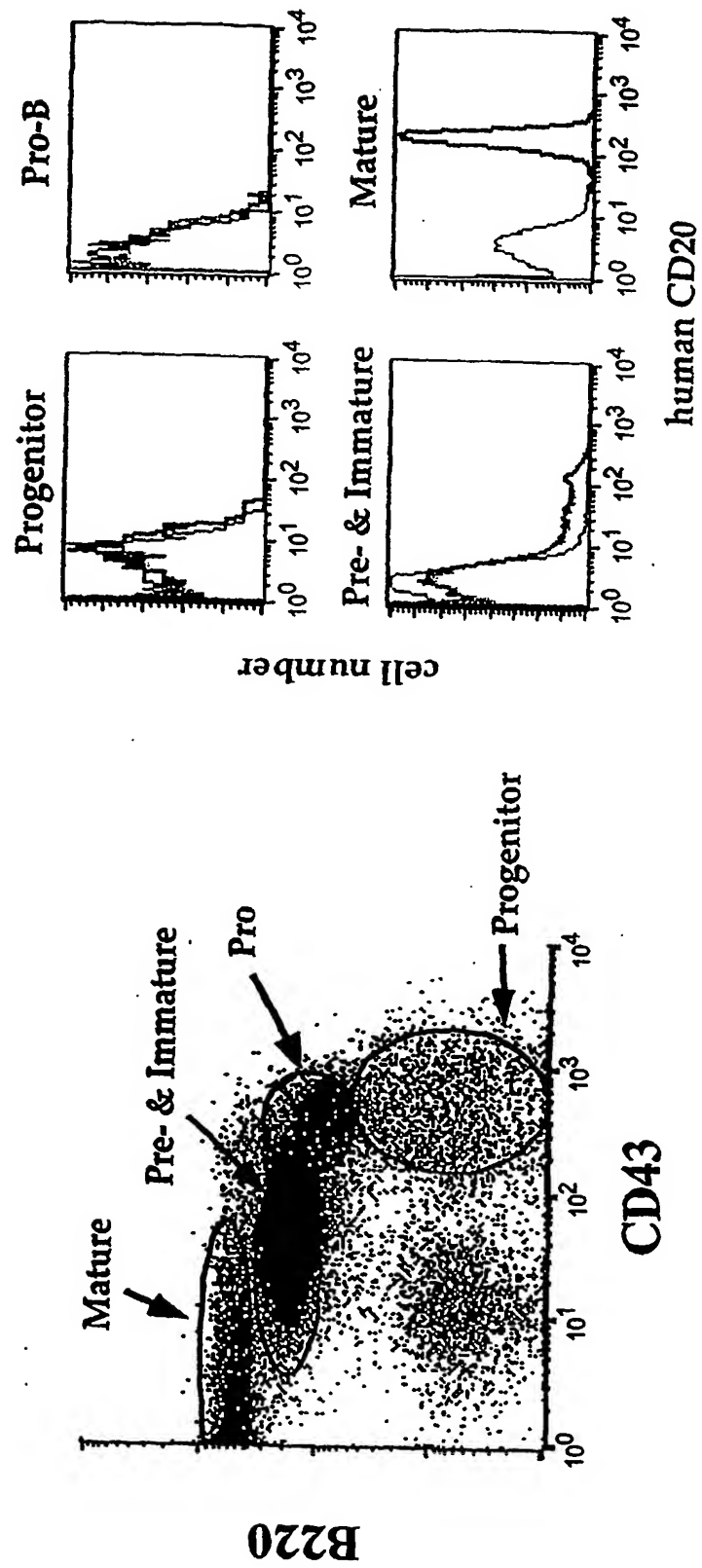


Figure 3

# Expression of human CD20 in Tg<sup>+</sup> mouse splenic B cells

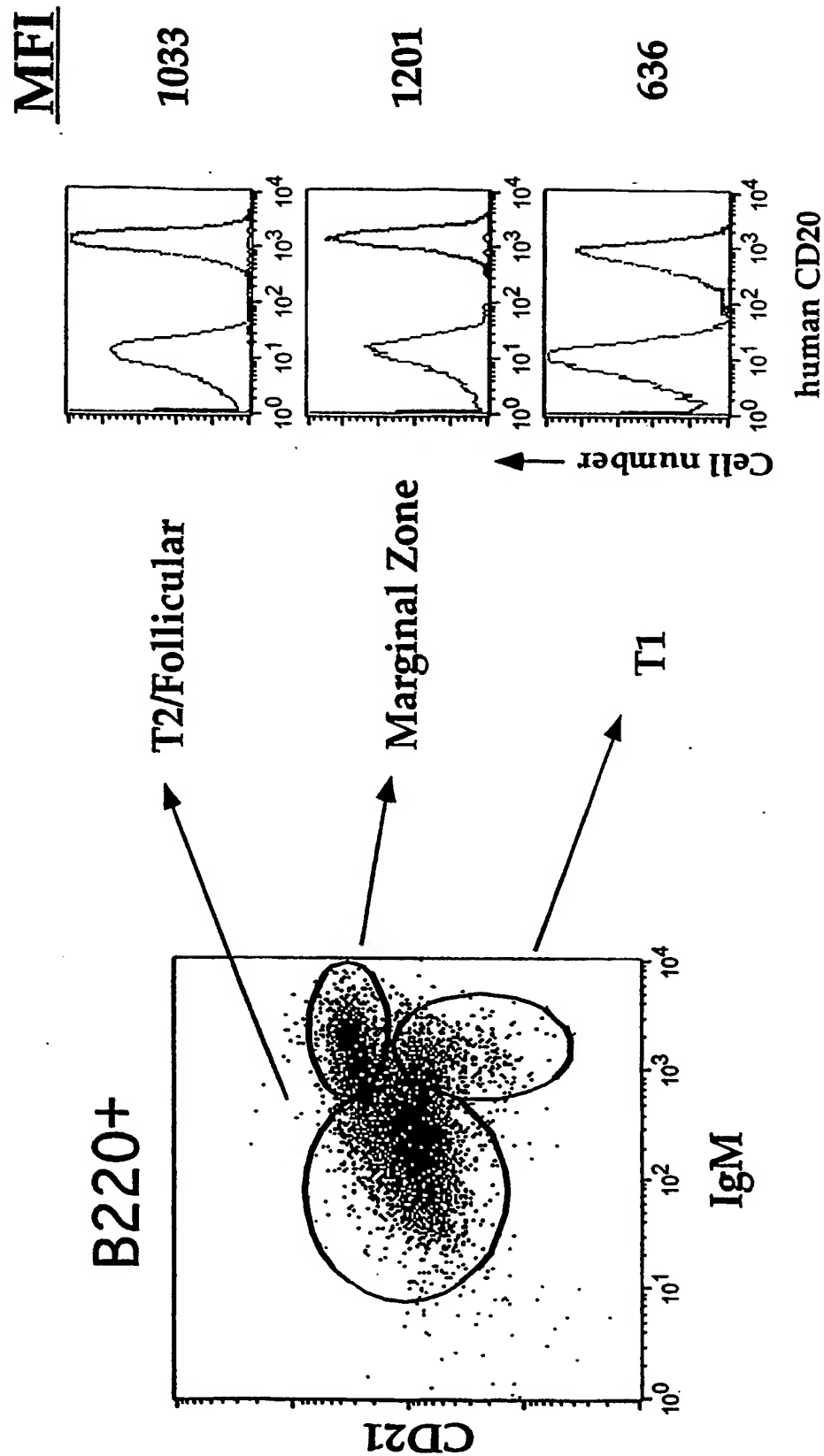


Figure 4

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# Expression of human CD20 in Tg<sup>+</sup> mesenteric LNs

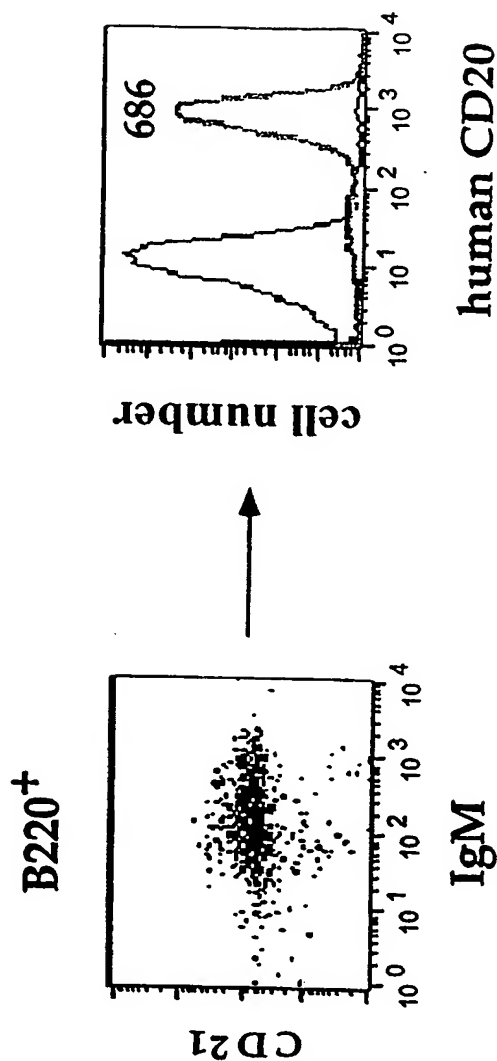


Figure 5

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# Expression of human CD20 in Tg<sup>+</sup> Peyer's Patches

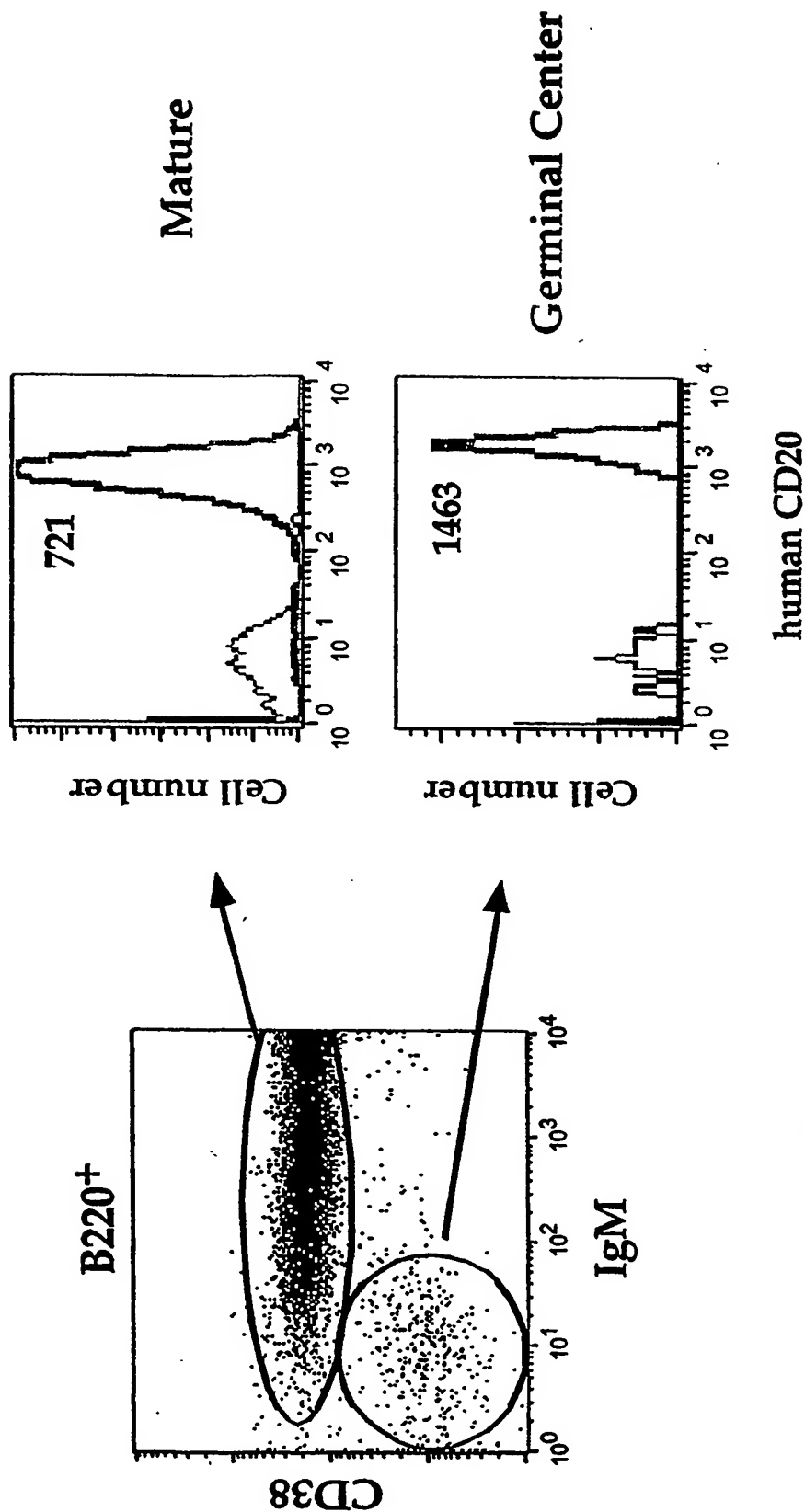
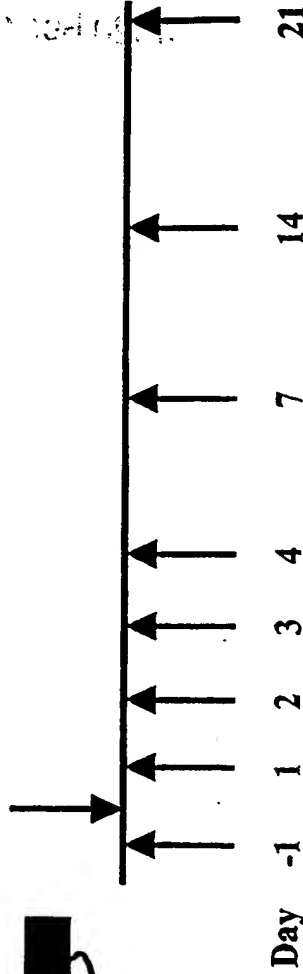
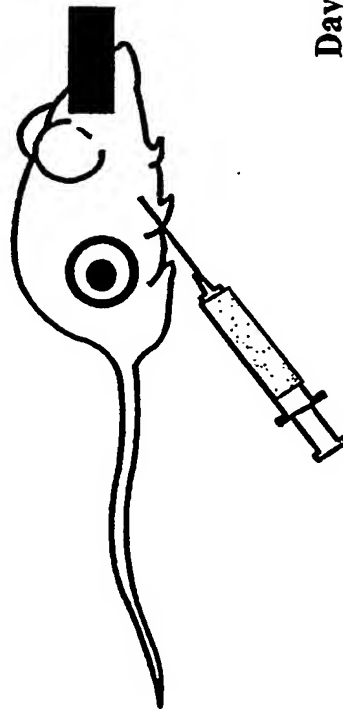


Figure 6

# Effects of anti-CD20 mAb in mice

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1.0 mg anti-CD20 mAb [ $\approx$ 50 mg/kg; 3.5 gm for 70 kg man]



FACS  
Peripheral Blood  
Spleen  
LN  
Bone Marrow  
Peyer's Patch  
Serum levels of anti-CD20 mAb

Figure 7

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# Depletion of peripheral B cells with anti-CD20 mAbs

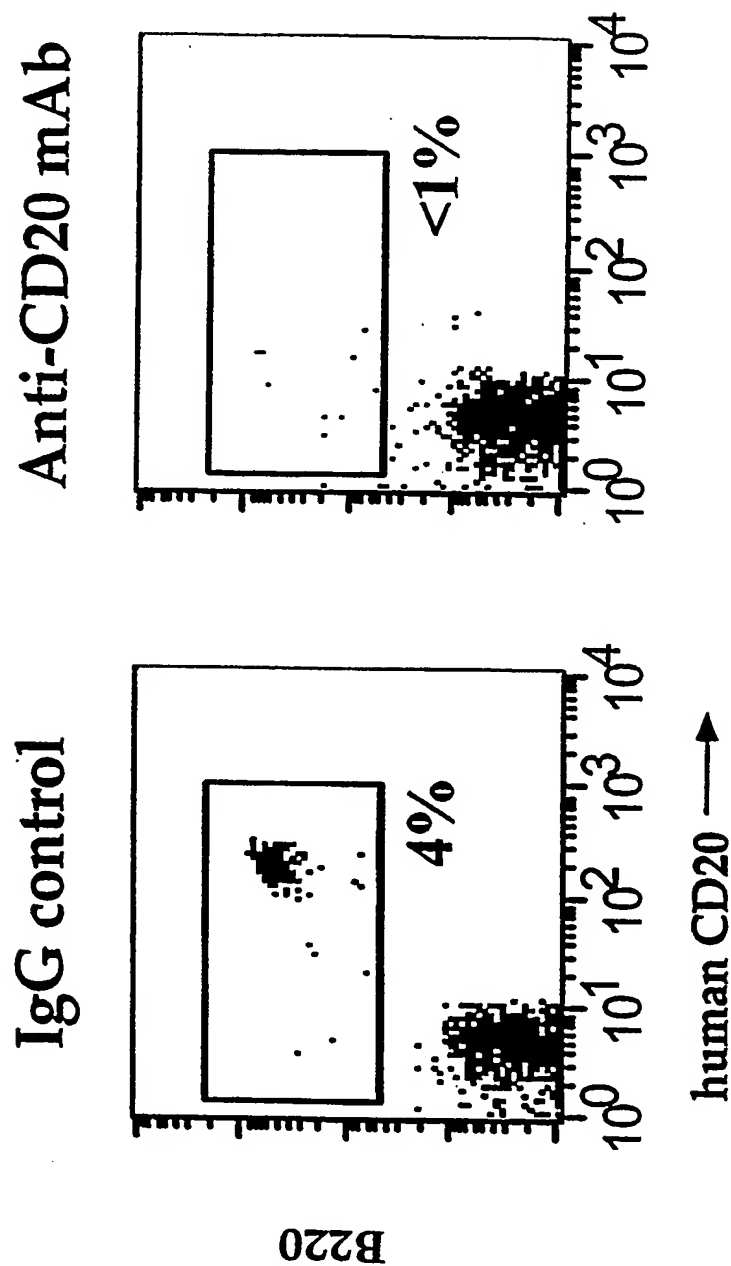


Figure 8



# Depletion of mature peripheral LN B cells by anti-CD20 mAb

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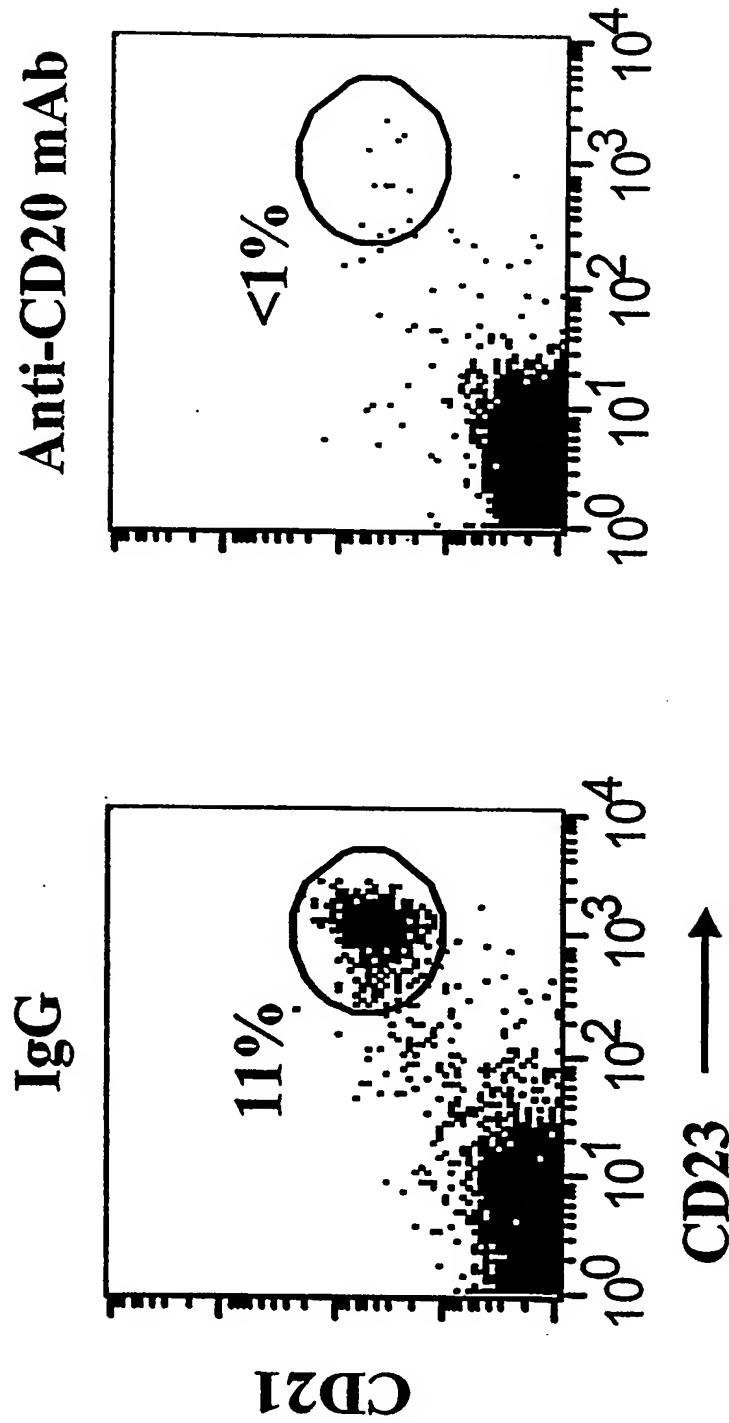


Figure 9

# Depletion of splenic T2 B cells by anti-CD20 mAbs

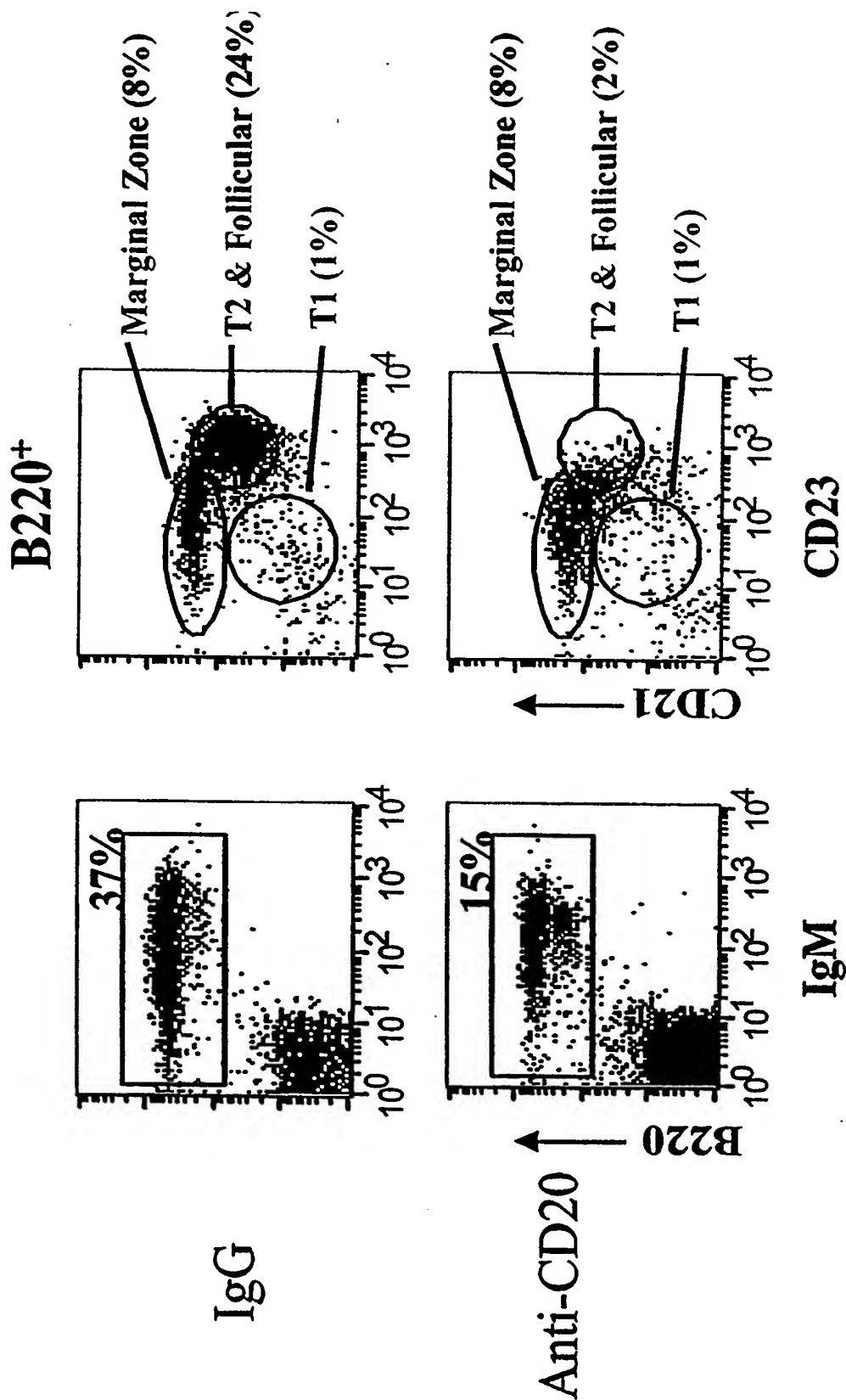


Figure 10

# Depletion of re-circulating mature B cells by anti-CD20 mAbs

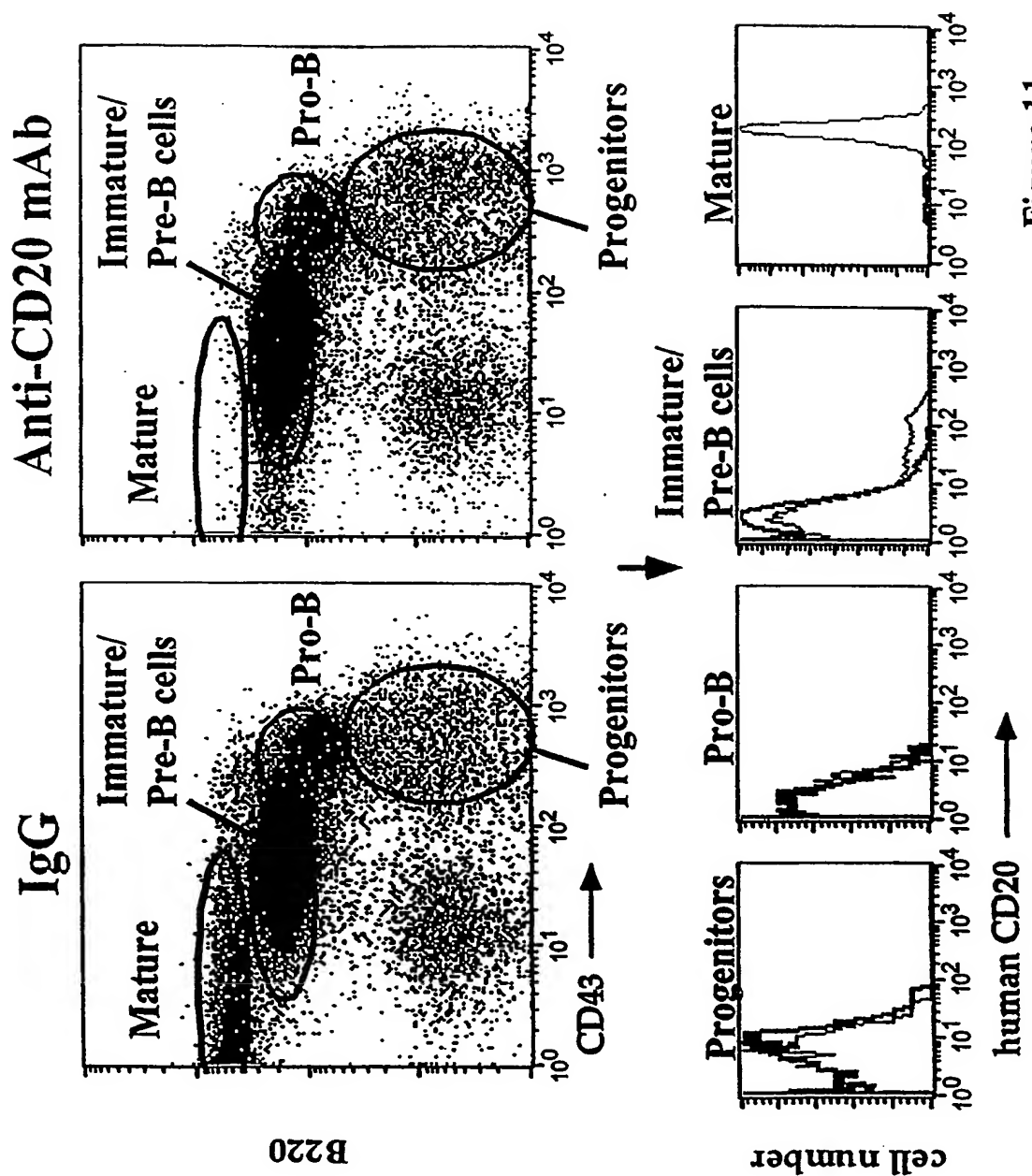


Figure 11

# Resistance of Peyer's Patches Germinal Center B cells to anti-CD20 mAbs

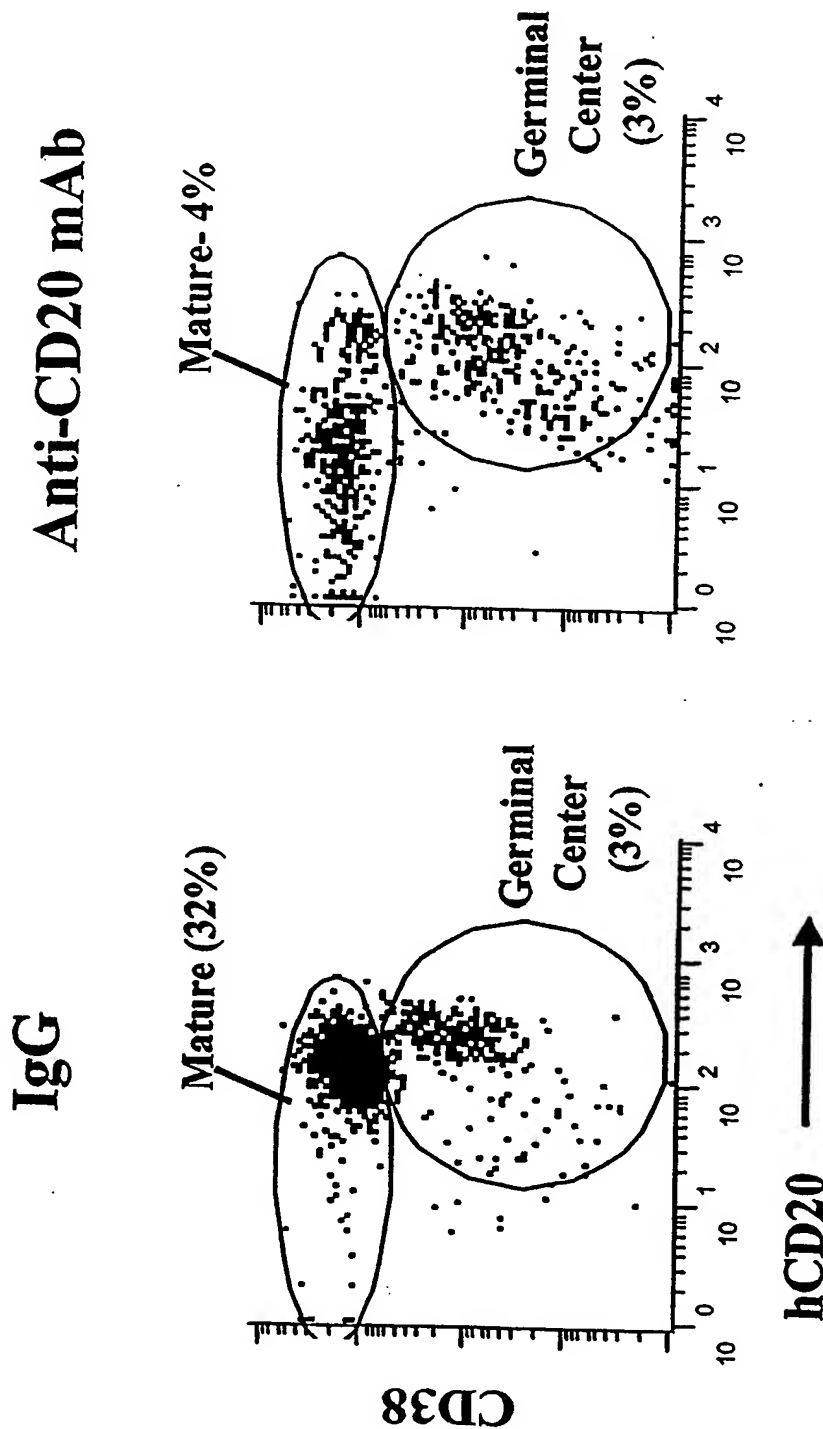


Figure 12

# Depletion & Recovery of B cells following anti-CD20 mAb Rx

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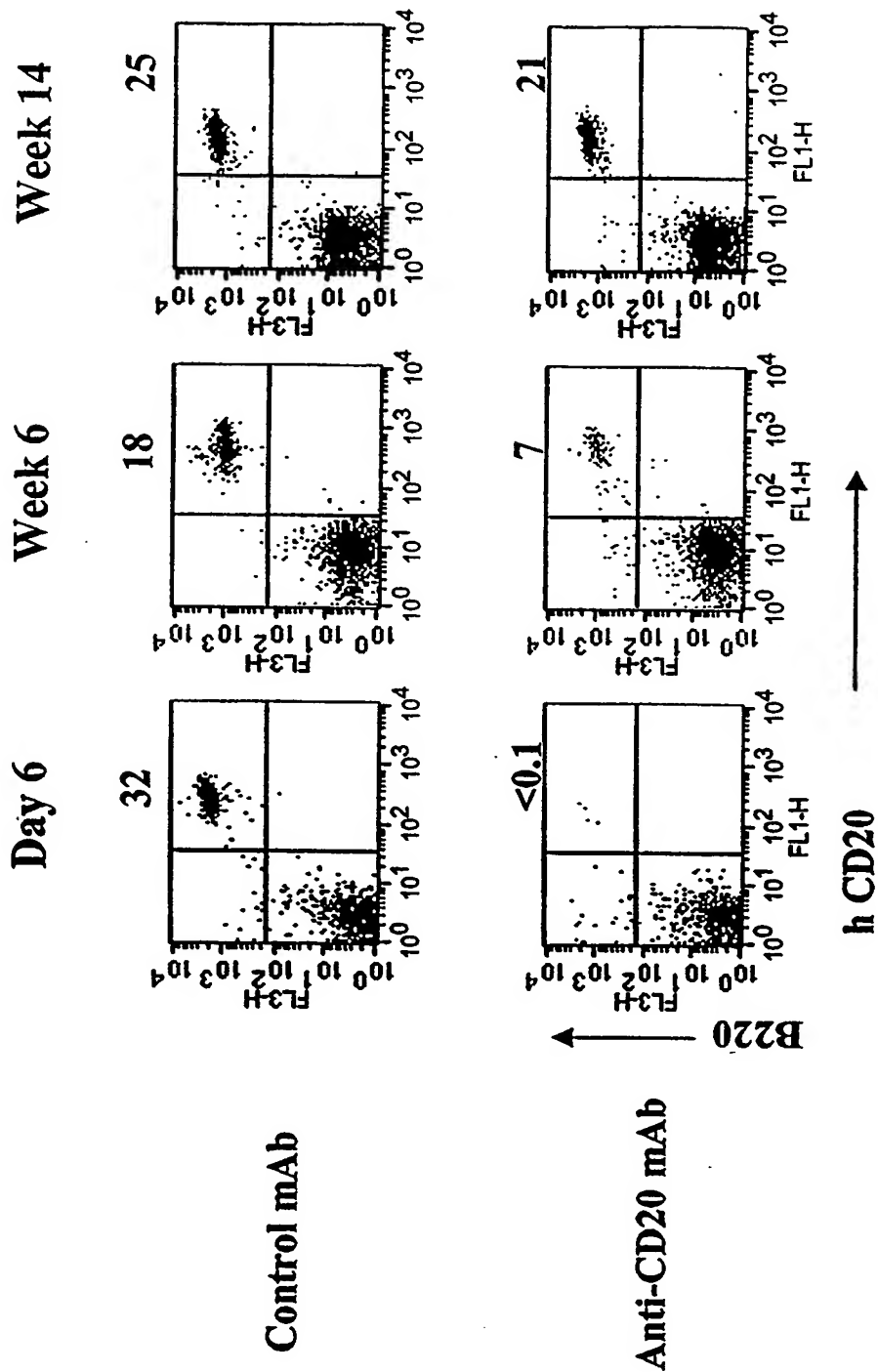
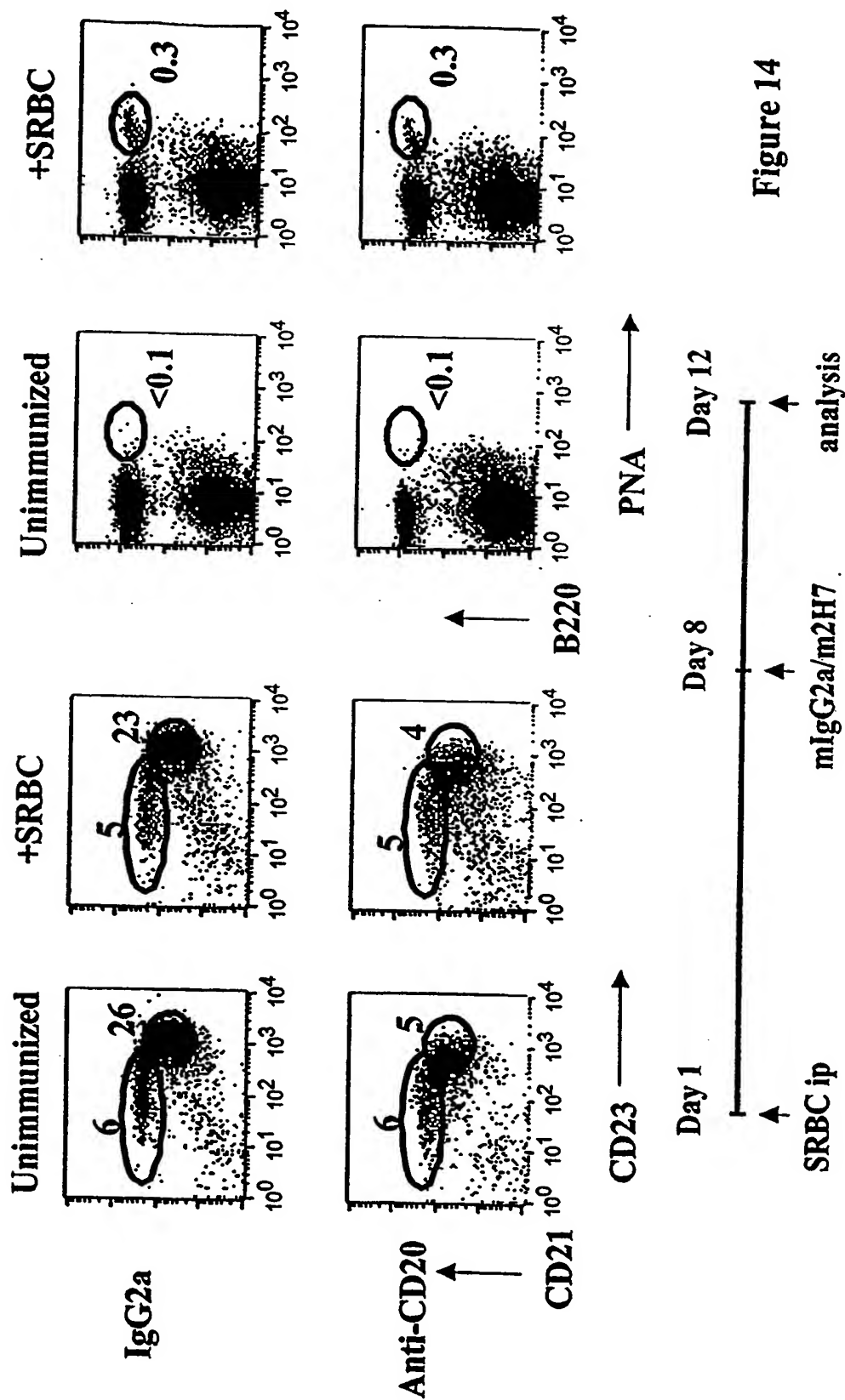


Figure 13

# Resistance of Splenic Germinal Center B cells to short-term anti-CD20 mAb Rx



# Non-depleted MZ and B1 B cells confer protection to T-Independent antigens

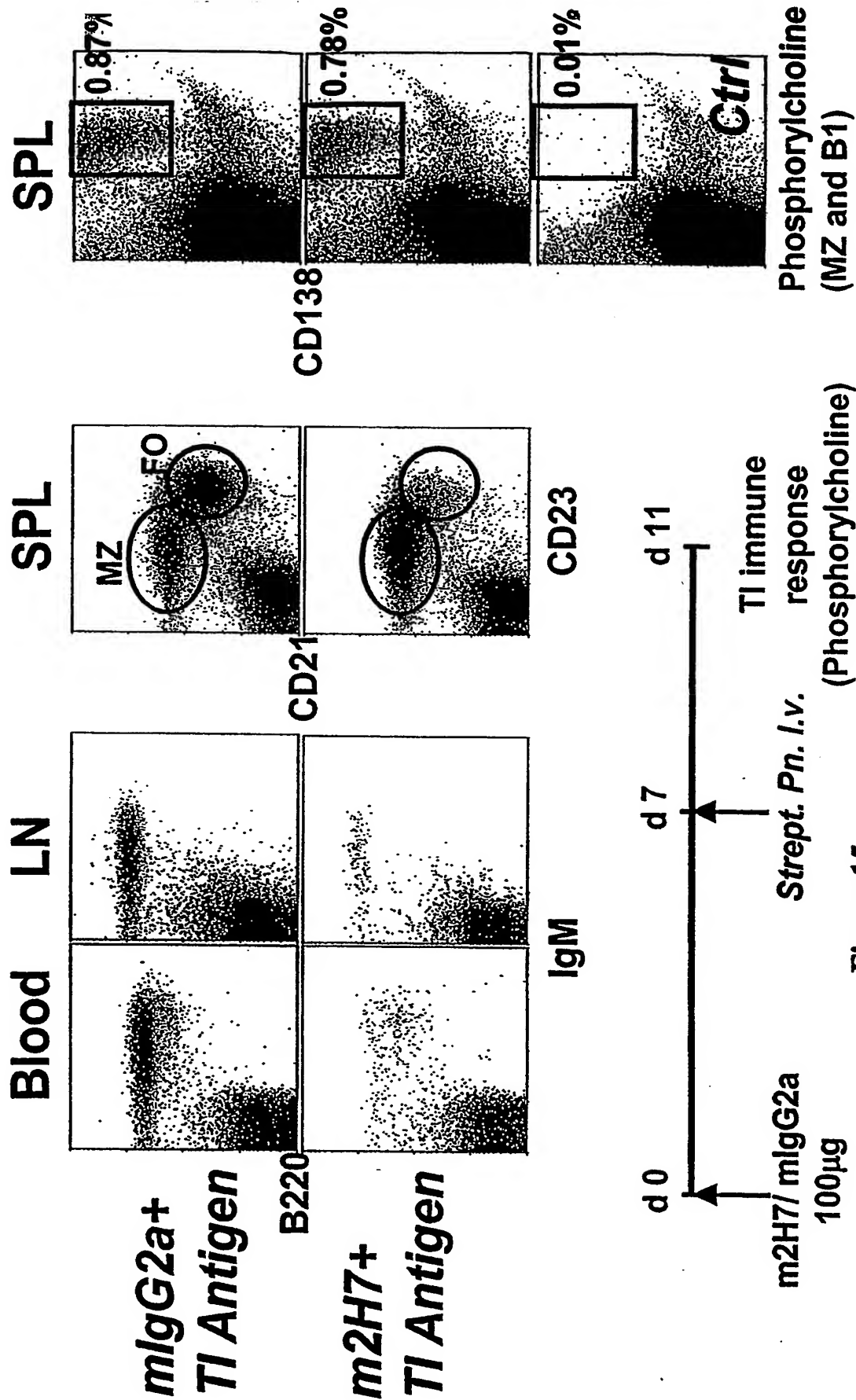


Figure 15

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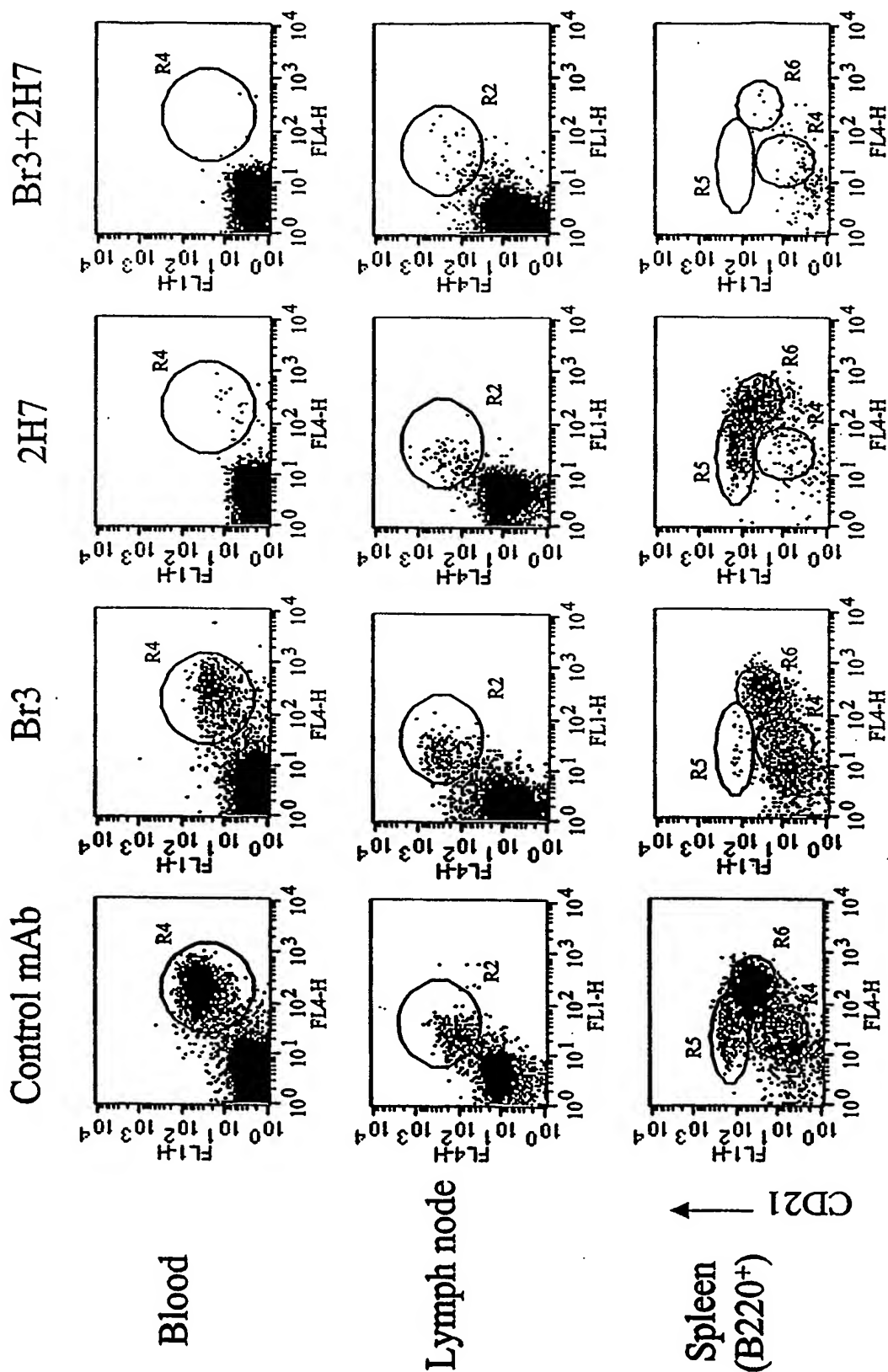


Figure 16



10,537,963

# In Peyer's Patches

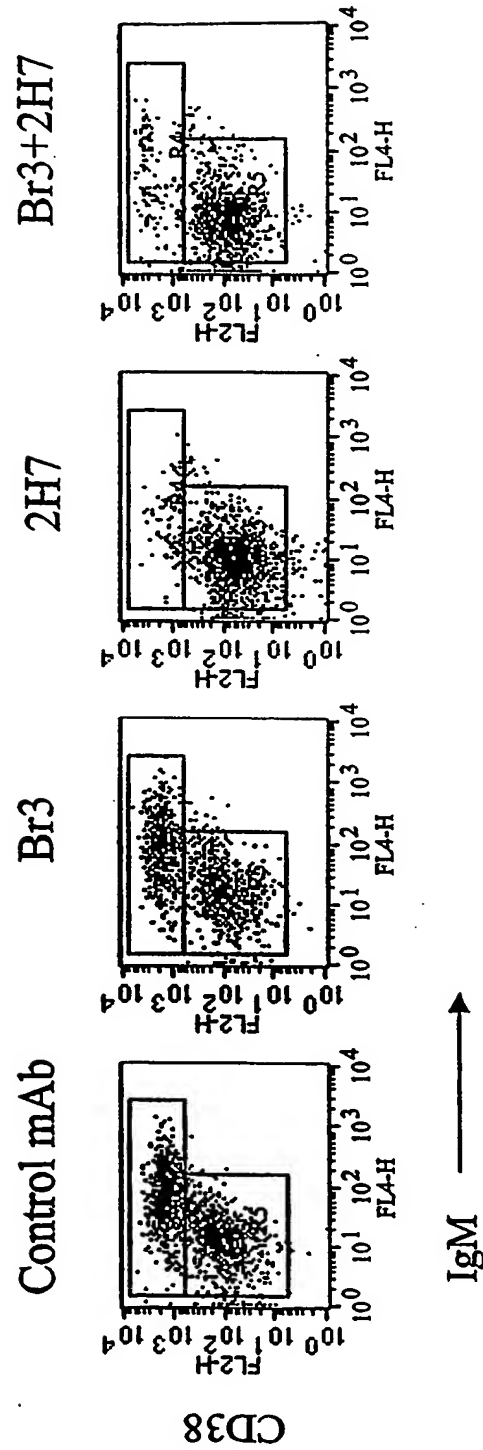


Figure 17

# Plasma cells are not depleted following long-term anti-CD20 mAb treatment

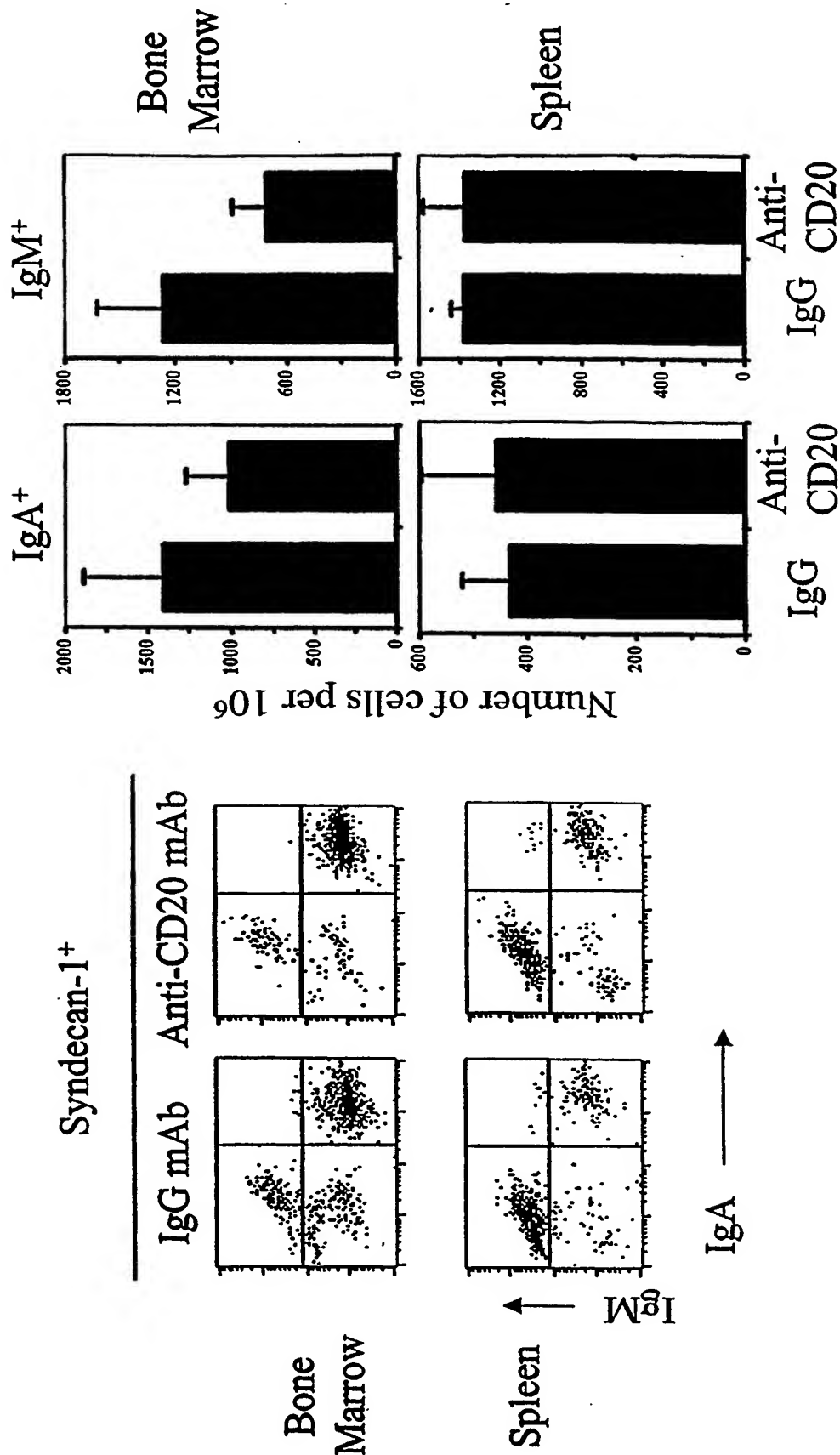
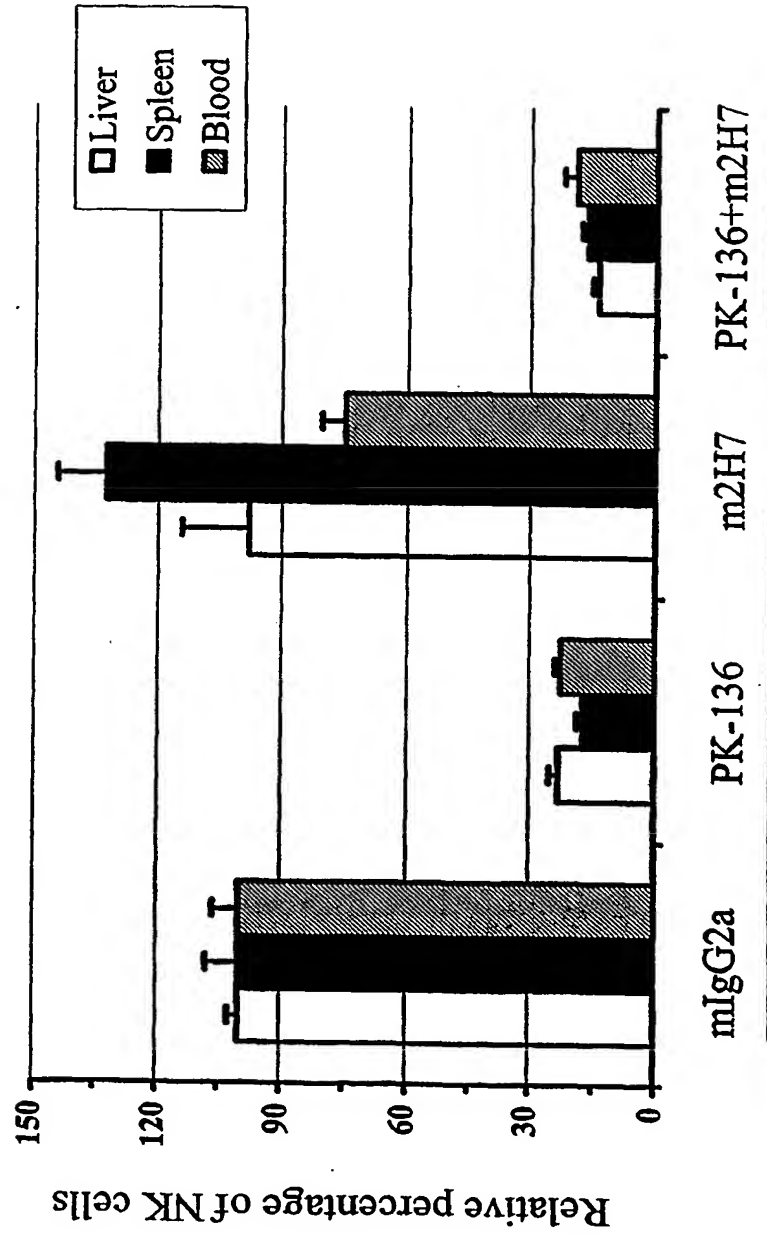


Figure 18

# Depletion of NK cells by PK-136 mAb



ip mAbs

Figure 19

# NK cells play a role in 2H7-mediated B cell depletion

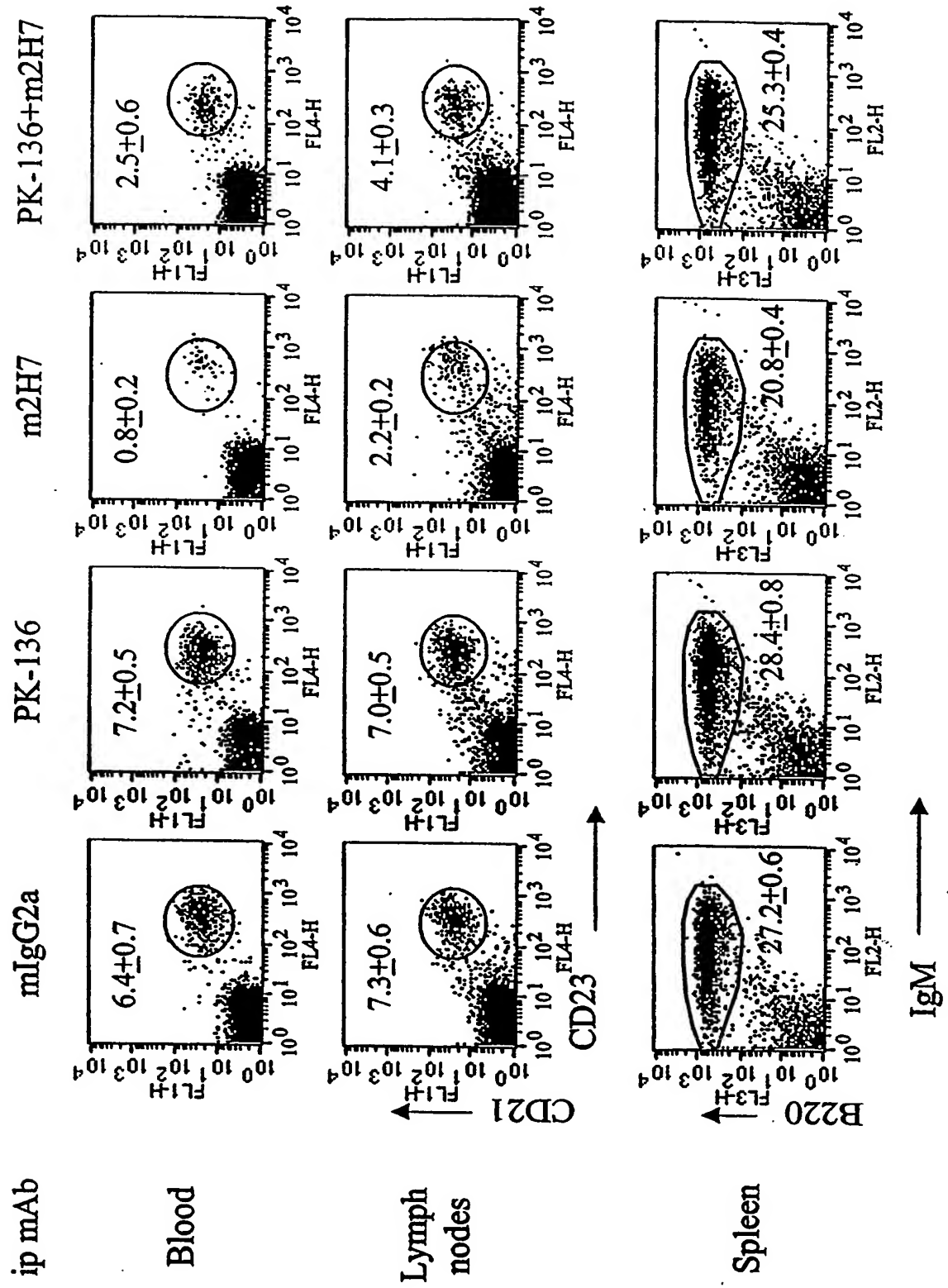
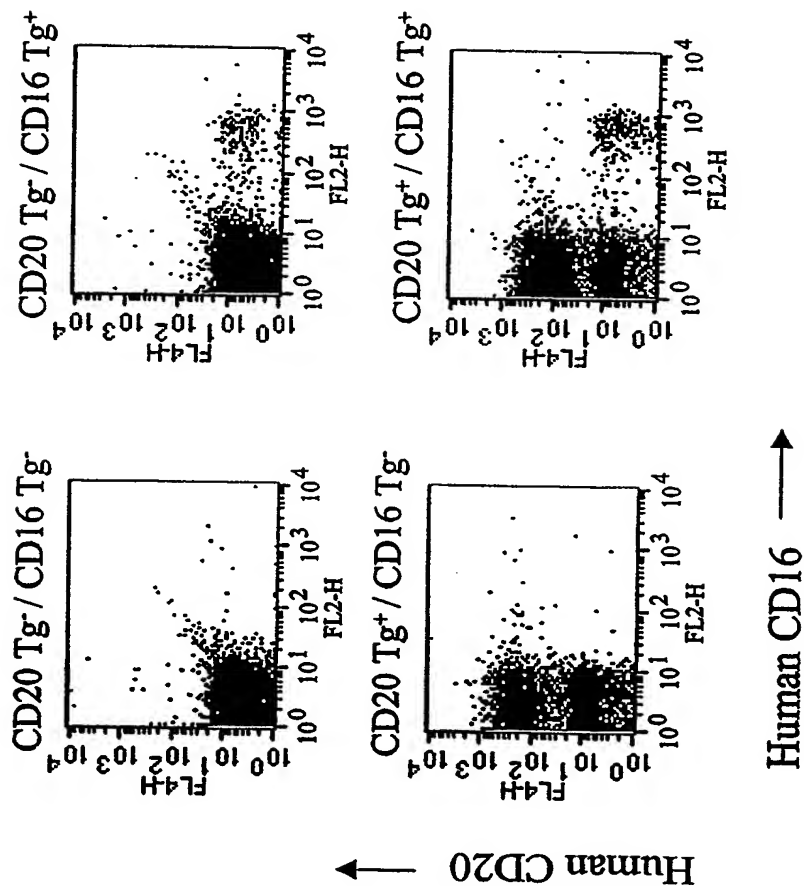


Figure 20

FIGURE 21

# Expression of Human CD20 and CD16 Transgenes



## FIGURE 22A

MGGGAGERLFTSSCLVGLVPLGLRISLVTCPLQCGIMWQLLLPT  
ALLLLVSAGMRTEDLPKAVVFLEPQWYRVLEKDSVTLKCQGAYS  
PEDNSTQWFHNESL ISSQASSYFIDAATVDDSGEYRCQTNLSTL  
SDPVQLEVHIGWLLLQAPRWVFKEEDPIHLRCHSWKNTALHKVT  
YLQNGKGRKYFHHNSDFYIPKATLKDSGSYFCRGLVGSKNVSSE  
TVNITITQGLAVSTISSFFPPGYQVSFCLVMVLLFAVDTGLYFSVKT  
NIRSSTRDWKDHKFKWRKDPQDK

## FIGURE 22B

1 gattctgtgt gtgtctcag atgtcagcc acagacctt gagggagtaa agggggcaga  
61 cccacccacc ttgctccag gctcttct tctgtgtct gtctatgtt ggggtccct  
121 tgccagactt cagactgaga agtcagatga agttcaaga aaaggaaatt ggtgggtgac  
181 agagatgggt ggaggggctg gggaaaggct gttacttcc tctgtctag tcggttgg  
241 cccttaggg ctccgatat ctttggtgac ttgtctctc cagtgtggca tcatgtgca  
301 gctgtctct ccaactgtc tgtacttct agttcagct ggcatgcga ctgaagatc  
361 cccaaaggct gtggtgtcc tggagccta atggtacagg gtgtcgaga aggacagtgt  
421 gactctgaag tgccaggag cctactccc tggagacaat tccacacagt ggttcacaa  
481 tgagagcctc atctcaagcc aggcctcag ctactcatt gacgtgcca cagtgcaga  
541 cagtggagag tacaggtgcc agacaaacct ctccaccctc agtgaccgg tgcagctaga  
601 agtcatac ggctggctgt tgtccaggc cctcgggtg gtgtcaagg aggaagacc  
661 tattcacctg aggtgtcaca gctggaagaa cactgtctg cataaggta cataattaca  
721 gaatggcaaa ggcaggaagt atttcatca taattctgac ttctacatt caaaagccac  
781 actcaaagac agcggctct acttctcag ggggttgtt gggagtaaaa atgtgtctc  
841 agagactgt aacatcacca tcaactaagg ttggcagtg tcaacctct catcattct  
901 tccacctggg taccaagtct ctttctgtt ggtgatgga ctcttttg cagtggacac  
961 aggactatat ttctctgtga agacaaacat togaagctca acaagagact ggaaggacca  
1021 taaatttaaa tggagaaagg accctcaaga caaatgacct ccatcccatg ggggtaataa  
1081 gagcagtagc agcagcatct ctgaacattt ctctggattt gcaaccctat catcctcagg  
1141 cctctctaca agcagcagga aacatagaac tcagagccag atccctatc caactctga  
1201 ctttctctg gtctccagt gaaggga aaa gccatgatc ttcaagcagg gaagccccag  
1261 tgagtagctg cattctaga aatgaagtt tcagagctac acaaacactt ttctgtccc  
1321 aaccgttccc tcacagcaa gcaacaatac aggctaggga tgtaatcct taaacatac  
1381 aaaaattgct cgtgttataa attaccagtt tttagggga aaaaaaaca attattcta  
1441 aataaatgga taagtagaat taatggtga ggcaggacca tacagagtgt gggaactgt  
1501 ggggatctag ggaattcagt gggaccaatg aaagcatggc tgagaaatag caggtagtcc  
1561 aggatagtct aaggagggtg ttccatctg agcccagaga taagggtgtc ttctagaac  
1621 attagccgta gtggaattaa caggaaatca tgagggtgac gtagaattga gtctccagg  
1681 ggactctatc agaactggac catctcaag tatataacga tgagtctct taatgctagg  
1741 agtagaaaat ggtcctagga aggggactga ggattgcgtt ggggggtgg gtggaaaaga  
1801 aagtacagaa caaacctgt gtcactgtcc caagtgtc agtgaacaga actatctcag  
1861 catcagaatg agaaagcctg agaagaaaga accaaccaca agcacacagg aaggaaagcg  
1921 caggagggtga aaatgcttc ttggccagg tagtaagaat tagaggtaa tgcagggact  
1981 gtaaaaccac ctttctgt tcaatatcta attctgtgt agcttgttc attgcattta  
2041 taaacaaat gttgtataac caatactaaa tgtactact agcttcgtc agttaagtta

**FIGURE 22B**  
**(CONT'D)**

2101 tgaaactttc aaatccttca tcatgtcagt tccaatgagg tggggatgga gaagacaatt  
2161 gttgcttatg aaagaaagct ttagctgtct ctgttttgta agctttaagc gcaacatttc  
2221 ttggttccaa taaagcattt tacaagatct tgcattgctac tcttagatag aagatgggaa  
2281 aaccatggta ataaaatag aatgataaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa  
2341 a



## FIGURE 22C

1 aagcttccca tctgttgca gtcccttact ctctctctgt gctctctct cttcttcta  
61 tctagccac ccttttgga gctaagaatt cctccctcca ttggagagcc acagaccaa  
121 gaggagtcaa ataagaaaat aagacctcaa agaaggaaaa caaagtgaag gccttgcac  
181 agaagtcacg tggcagaaag ccacctggat atctgaaaag aagaaagaat tgagggatat  
241 ccgcttttg cctcagagac catccttagc cctgaaggct ttgtttctgc ttaggtttc  
301 ccagataagc atccgaagtg ctacagcaag gaactttaag ttccagata ctgtctgga  
361 ttttgcaagg cgtagatgag tcacttgaga aggagaactg gaatggctgc ctaggttcat  
421 ttccattgtg caatccaagg gcctgtggag aaggggctgc tgcaagactc tgtgtgtggc  
481 ggggggaggg gtgggtacgt ggatggcaat gggaggatca attactcca cccaggagcc  
541 aaatgaaaca cacaataaa aaacaaaacc tgagtagtgg ttttaggtc attctggagt  
601 agaaagagca ttcatttata gcaaagggtg gcgggcacct gtgtcagccc ctgcctccac  
661 tccaccctca acaagtatca ggtgccaca cgggcctgct gctgcctcc tgggctttc  
721 taagccaggt gagacctgic ccagatgtcc acgaatccac tgggggagtg gcactatcaa  
781 gcagagtcac ctgattttct gcctgggacc tggaccattg tgagagtaac caacgtgggg  
841 ttacggggga gaatctggag agaagagaag aggttaacaa cctccact tctgtgccac  
901 cccctccac cttttctggt aaggagccct ggagccccgg ctctaggct gacagaccag  
961 cccagatcca gtggcccga ggggcctgag ctaaaccgc aggacctggg taacagagg  
1021 aaggtaaaga gtctctgctc tgcacctcc ccacccccc cttttctgt atctttcag  
1081 cctttcgtg gtgactgtt ctccagggc ccatttctct accctacctg ggtttctct  
1141 aacctgaaa tctaatgac aaatcacact aaaaagtcag tagctctgt ggattacata  
1201 tccaggagc atatagatt tgaatttga atttgaaag aaattctgcg tggagataat  
1261 attgaggcag agacactgct agtggctga agattgaaa ggaccactt ctgtgtgac  
1321 gcagggcctc agctggagat agatgggtct gggcgaggca ggagagtac aagtctgag  
1381 gtgaaatgaa ggaagccctc agagaatgct cctccacct tgaatctcat cccagggtc  
1441 tcactgtccc attctggtg ctgggtggat ccaaaccag gagatggggc aagcatcctg  
1501 ggatggctga gggcacactc tggcagattc tgtgtgtgc ctacatgct cagccacaga  
1561 cctttgaggg agtaaagggg gcagaccac ccacctgccc tccaggctct ttccttctg  
1621 gtctgttct atggtggggc tcccttgcca gactcagac tgagaagica gatgaagtt  
1681 caagaaaagg aaattggtg gtgacagaga tgggtggagg ggctggggaa aggtgttta  
1741 ctctctctg tctagtcgtt ttgtccctt tagggctccg gatattctg gtgactgtc  
1801 cactccagtg tggcatcatg tggcagctgc tctcccaac tgctctgcta ctctaggta  
1861 agtcagggc tccctggtg agggagaagt ttgagatgcc ttgggttcag cagagacccc  
1921 tttcaggct acgaatgaga ctcacagaa gggatgggac cctcaccac atctatagct  
1981 gtggattgag ctctaggac aagccaagat ggggctagaa atgaggagaa tgctgttcc  
2041 aattggggca tactcatgag tgaggccagt cactcacc cctgtggctc cagaatcact

**FIGURE 22C**  
**(CONT'D)**

2101 ctgtggaacc aaagagcttc gactagatgg tccctagggt ctgtctcttt cagtttgaca  
2161 ttccaggggt ctctctatg attttcaatt tctaccttt ctgtgggga tatgggtga  
2221 ggctctttct gtagcttgg ttagggaaat tcaacctgta cccttaatt gtgagttgc  
2281 acagggagca aggggtaagg gagcagtgt gaaaataggg atttgtgtg acagtggcg  
2341 aagaggcatg aacagtggag accagagagc aggtagcaag gttccacca gaaacatcct  
2401 gattcttggg aaaattgggc tccctgggca gaggagggca ggggagtttt aaactcactc  
2461 tatgttctaa tcactctgat ctctgcccct actcaatatt tgatttactc tttttcttg  
2521 cagtttcagc tggcatgagg actggtgagt cagcttcag gtcttgatt gacccagtgg  
2581 ggcacatatg gggacaaagg ccataagata ttgggaaatg ctgttgaat gggaaaatgc  
2641 tgatgtgggg ttagcagga tagttcctcc aacacagcag aacttggccc tgtgcttctc  
2701 tggccagctt tccctaagat actgaacagg ccaaaaatgg ggccaagatg ctctaagact  
2761 gagccaccaa gcatgggtt gcaatgagct cattctggct ttgaggctcc ctgggaatgg  
2821 cagtgtagag cctgctctc tccctgtcct caccacat tatcttggct cctcagaaga  
2881 tctcccaaag gctgtggtgt tctggagcc tcaatgttac aggggtgctg ag

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Figure 22D  
Mouse CD16 alpha chain

1 gtagtcac tcctgaacct catcagactc tgatccaggt ctggaatgac ttggacacc  
61 cagatgttc agaatgcaca ctctggaagc caatggctac ttccaccact gacaattctg  
121 ctgctgttg ctttgcaga caggcagagt gcagctctc cgaaggctgt ggtgaaactg  
181 gacccccat ggatccaggt gctcaaggaa gacatggtga cáctgatgtg cgaagggacc  
241 cacaacctg ggaactctc taccagtggt ttccacaacg ggaggtccat ccggagccag  
301 gtccaagcca gttacacgtt taaggccaca gtcaatgaca gtggagaata tgggtgtcaa  
361 atggagcaga ccgcctcag cgacctgta gatctgggag tgatttctga ctggctgctg  
421 ctccagaccc ctacgagggt gttctggaa ggggaaacca tcacgctaag gtgcatagc  
481 tggaggaaca aactactgaa caggatctca ttctccata atgaaaaac cgtgaggtat  
541 catcactaca aaagtaatt ctctatccca aaagccaacc acagtcacag tggggactac  
601 tactgcaaag gaagtctagg aagtacacag caccagtcca agcctgtcac catcactgtc  
661 caagatccag caactacatc ctccatctct ctagtctgtt accacactgc ttctcccta  
721 gtgatgtgcc tctgtttgc agtggacacg ggcctttatt tctacgtacg gagaaatctt  
781 caaaccocga gggagtactg gaggaagtcc ctgtcaatca gaaagcacca ggctcctcaa  
841 gacaagtgc acccatcca tcctatggca aaacatacga tgttttggtg gcagcagcaa  
901 ctttcagcc acacagcctt ccttgaaag caacttaca gcaggccggg atgtttggtt  
961 ctcaatcac aacgacttag gatcaccagt tcaaggcttg ctgggtcaca cagagagagt  
1021 gagtgcaagt ctagcctgga taaccagtg agatcctggg tttaggcggc tcatcaggaa  
1081 agagaacctg ttgctaatt cacaacaag atgcctactg cccatgtggc caaaggagag  
1141 aacaaggcc tggaggtgt cctctgacct ccacatcca ccatggcagg tgcacacaat  
1201 aaattaaaat gtcatgtata ttttaaaaca agagacaggg gcaggctaag ggtgatggc  
1261 atagctgtta tccagtacac ataatgcctt gggtttgacc tcctataata aagc

Figure 22E  
CD16 alpha chain-B

MWQLLLPTALLLVVSAGMRTE<sup>1</sup>LPKAVWFLEPQWYSVLEKDSVT  
LKCQGAYSPEDNSTQWFHNESLISSQASSYFIDAATV<sup>2</sup>NDSGEYR  
CQTNLSTLSDPVQLEVHIGWLLLQAPRWVFKEEDPIHLRCHSWK  
NTALHKV<sup>3</sup>TYLQNGKDRKYFHHNSDFHIPKATLKDSGSYFCRGLV  
GSKNV<sup>4</sup>SSETVNITITQGLAVSTISSFSPPGYQVSFCLVMVLLFAVD  
TGLYFSV<sup>5</sup>KTN

1 tctttggtga cttgtccact ccagtg<sup>6</sup>tggc atcatgtggc agctgtcct cccaactgct  
61 ctgctacttc tagtttcagc tggcatg<sup>7</sup>cgg actgaagatc tcccaaaggc tgtggtgttc  
121 ctggagcctc aatggtacag cgtgctgag aaggacagtg tgactctgaa gtgccaggga  
181 gcctactccc ctgaggacaa ttccacacag tggttcaca atgagagcct catctcaagc  
241 caggcctcga gctacttcat tgacgtgcc acagtcaacg acagtggaga gtacaggtgc  
301 cagacaaacc tctccaccct cagtga<sup>8</sup>cccg gtgcagctag aagtccatat cggctggctg  
361 ttgctccagg cccctcgg<sup>9</sup>tg ggtgttcaag gaggaagacc ctattcacct gaggtgtcac  
421 agctggaaga acactgctct gcataagg<sup>10</sup>tc acatat<sup>11</sup>tac agaatggcaa agacaggaag  
481 tattttcatc ataattctga cttccacatt ccaaaagcca cactcaaaga tagcggctcc  
541 tacttctgca gggggctgt tgggag<sup>12</sup>taaa aatgtgtctt cagagactgt gaacatcacc  
601 atcactcaag gtttggcagt gtcaaccatc tcatcattct ctccacctgg gtaccaagtc  
661 tcttctgct tgg<sup>13</sup>tatgg<sup>14</sup>t actcctttt gcagtggaca caggactata ttctctgtg  
721 aagacaaaca tt<sup>15</sup>gaagctc aacaagagac tggaaggacc ataaact<sup>16</sup>taa atggagaaag  
781 gaccctcaag acaa<sup>17</sup>atgacc cccatcccat gggagtaata agagcagtgg cagcagcatc  
841 tctgaacatt tctctggatt tgca<sup>18</sup>accca tcatcctcag gcctctc

Figure 22F

1 aagcttccca tctgttgca gtcccttact ctctctctgt gctctctct cttcttcta  
61 tctagcccac ccttttgta gctaagaatt cctccctcca ttgagagtc acagaccaa  
121 gaggagtcaa ataagaaaat aagacctcaa agaaggaaaa caaagtgaag gccttgcac  
181 agaagtcacg tggcagaaag ccacctggat atctgaaaag aagaaagaat tgagggat  
241 ccgcttttg cctcagagac catccttagc cctgaaggct ttgttctgc tttaggtttc  
301 ccagatgagc atctgaagtg ctacagcaag gaacttcaag ttccagata cttgtctga  
361 ttttgaagg cgtagatgag tcaactgaga aggagaactg gaatggcggc ctgggttcat  
421 ttccgttggt caatccaagg gcctgtggag aaggggctgc tgcaagactg tgtgtgtggc  
481 agggggaggg gtgggtacgt ggatggcaat gggaggatca attaactcca cccaggagcc  
541 aaatgaaca cacaataaa aaacaaaacc tgagtagtgg ttttaggtc attctggagt  
601 agaaagagca ttcattata gcaaagggtg gcgggcacct gtgtcagccc ctgcctccac  
661 tccacccta acaagtatca ggtgccaca cgggcctgct gctgcctcc tgggctttc  
721 taagccaagt gagacctgtc ccagatgtcc acgaatccac tgggggagtg gcactatcaa  
781 gcagagtcac ctgattttct gcctgggacc tggaccattg tgagagtaac caacatgggg  
841 ttacggggga gaatctggag agaagagaag aggttaacaa cctccact tctggccac  
901 cccctccac cttttctgtt aaggagccct ggagccctgg agccctggct cctaggctga  
961 cagaccagcc cagatccagt ggcccggagg ggccctgagct aaatccgcag gacctgggta  
1021 acacgaggaa ggtaaagagt tctgtcctc acccctcccc accccacct tttctgtgat  
1081 ctttcagcc tttactggt gactgttct tccaggggccc atttctctac cctacctggg  
1141 tttctctaa cctggaaatc taatgatcaa atcacactaa aaagtcagct cctgtggatt  
1201 acatatccca ggagcatata gattttgaat ttgaatttt gaaagaaatt ctgcgtggag  
1261 ataattatga ggcagagaca ctgctagtgg tcaaagattt gaaaggacaa ctttctgtg  
1321 gcaggcaggg cctcggctgg agatagatgg gtctggacga ggcaggagag tgagaagttc  
1381 tgaggtgaaa tgcaggaagc cctcagagaa tgctcctccc accctgaatc tcatccccag  
1441 ggtcttgctg tccattctt ggtgctgggt ggatctaaat ccaggagatg ggggcaagca  
1501 tctgggaaag ctgagggcac actctggcag attctgtgtg tgcctcaga tgcctagccg  
1561 cagaccttg ggggagtaaa gggggcacac ccaccacct tgcctccagg ctcttctct  
1621 cctattctg ttctatgggt gggctccatt gcgagacttc agattgagaa atcagatgaa  
1681 gttcaagaa aaggaaactg gcaggtgaca gagatgggtg gagggactgg ggaaaggctg  
1741 ttactcct cctgtctagt cggcttggtc ctttagggc tccggatata tttggtgact  
1801 tgtccactcc agtgtggcat catgtggcag ctgctcctcc caactgctct gctactcta  
1861 ggtaagtcag gatattcctg gttaggggag aagtttgaga tgccttgggt tcatcagaga  
1921 cccctttca ggctacgaat gagactccca caaagggatg ggaccctca ccacatctat  
1981 agctgtggat tgagctacca ggacaagcca agatggggct agaaatgagg agaagtctgg  
2041 ttcaattgg gtcatagtca tgagtgggc cagtcacttc acccctctgg gtcccagaat

**FIGURE 22F**  
**(CONT'D)**

2101 cactatgtgg aactgaagag cttcgactag atggcccta gggctgtct cttcagttt  
2161 gacattccag ggttctctc tatggtttt aatttctacc ctttctgtg gggatatggg  
2221 ttgaggctgt ttctgtggct tggtttaggg aaattcaacc tgtaccctta atttgtgagt  
2281 ttgcacaggg agcaaggggt aaggaggcag tgtgaaaat agggatttgt gttgacagt  
2341 gcgcaagagg catgaacagt agagaccaga gaggcagtag caaggttcc accagaaaca  
2401 tctgattct tgggaaaatt gggctcctgg ggcagaggag ggcaggggag ttttaaactc  
2461 actctatgtt ctaatcactc tgatctctgc cccactcaa tatttgattt actctttttt  
2521 cttgcagttt cagctggcat gcggactggg gagtcagctt catggctctg gattgacca  
2581 gtggggcaca tatggggaca atggccataa gatattggga aatgcttgtt gaatgggaaa  
2641 atgctgatgt ggggttagca gggatagttc ctccaacaca gcagaacttg gccctgtgct  
2701 tctctggcca gctttcctta agatactgaa caggccaaaa atggggccaa gatgctctaa  
2761 gactgagcca ccaagcatgg gtttgcaatg agctcattct ggcttgagg ctccctggga  
2821 atggcagtgt agagcctgct cctctcctg tctcacccc acattatctt ggctcctcag  
2881 aagatctccc aaaggctgtg gtgttctctg agcctcaatg gtacagcgtg cttgagaagg  
2941 acagtgtgac tctgaagtgc caggggagcct actccctga ggacaattcc acacagtggg  
3001 ttcacaatga gaggctcatc tcaagccagg cctcgag

Figure 22G

Murine FcγRIII

1 gtagttcatc tcttgaacct catcagactc tgatccagtt ctggaatgac ttggacacc  
61 cagatgttc agaatgcaca ccttgaagc caatggctac ttccaccact gacaattctg  
121 ctgctgttg cttttgcaga caggcagagt gcagctcttc cgaaggctgt ggtgaaactg  
181 gacccccat ggtccaggt gctcaaggaa gacatggtga cactgatgtg cgaagggacc  
241 cacaaccctg ggaactcttc taccagtggt ttccacaacg ggaggtccat cggagccag  
301 gtccaagcca gttacacgtt taaggccaca gtcaatgaca gtggagaata tcggtgtcaa  
361 atggagcaga cccgcctcag cgacctgta gatctgggag tgatttctga ctggctgctg  
421 ctccagaccc ctacgagggt gttctggaa ggggaaacca tcacgctaag gtgcatagc  
481 tggaggaaca aactactgaa caggatctca ttctccata atgaaaaatc cgtgaggtat  
541 catcactaca aaagtaattt ctctatccca aaagccaacc acagtcacag tggggactac  
601 tactgcaaag gaagtctagg aagtacacag caccagtcca agcctgtcac catcactgtc  
661 caagatccag caactacatc ctccatctct ctagtctggt accacactgc ttctcccta  
721 gtgatgtgcc tctgtttgc agtggacacg ggcctttatt tctacgtacg gagaaatctt  
781 caaaccgccg gggagtactg gaggaagtcc ctgtcaatca gaaagcacca ggctcctcaa  
841 gacaagtgc acccatcca tctatggca aaacatacga tgttttggtg gcagcagcaa  
901 ctttcagcc acacagcctt cctttgaaag caacttaca gcaggccggg atgtttggtt  
961 ctcaatcac aacgacttag gatcaccagt tcaaggcttg ctgggtcaca cagagagagt  
1021 gagtgaagt ctacgctgga taaccagtg agatcctggg tttaggcggc tcatcaggaa  
1081 agagaacctg ttgctaattt cacaacaag atgcctactg ccatgtggc caaaggagag  
1141 aacaagggtc tgggaagttg cctctgacct ccaccatcca ccatggcagg tgcacacaat  
1201 aaattaaaat gtcatgtata ttttaaaaca agagacaggg gcaggctaag ggtgatggc  
1261 atagctgtta tccagtacac ataatgccct gggttgacc tctataata aagc

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## FIGURE 23A

MTTPRNSVNGTFPAEPMKGPIAMQSGPKPLFRRMSSLVGPTQSF  
FMRESKTLGAVQIMNGLFHIALGGLLMIPAGIYAPICVTWYPLWGGIMYIISGSLLA  
ATEKNSRKCLVKGMIMNSLSLFAAISGMILSIMDILNIKISHFLKMESLNFIRAHTP  
YINIYNCEPANPSEKNPSTQYCYSIQSLFLGILSVMLIFAFFQELVIAGIVENEWKR  
TCSRPKSNIVLLSAEEKKEQTIEIKEEVVGLTETSSQPKNEEDIEIPIQEEEEETE  
TNFPEPPQDQESSPIENDSSP"



## FIGURE 23B

1 agtgtgcttg agaaacaaac tgcacccact gaactccgca gctagcatcc aaatcagccc  
61 ttgagatttg aggccttgga gactcaggag tttgagagc aaaatgacaa caccagaaaa  
121 ttcagtaaat gggactttcc cggcagagcc aatgaaaggc cctattgcta tgcaatctgg  
181 tccaaaacca ctcttcagga ggatgtcttc actggtgggc cccacgcaaa gcttctcat  
241 gagggaatct aagactttgg gggctgtcca gattatgaat gggctctcc acattgccct  
301 ggggggtctt ctgatgatcc cagcagggat ctatgcaccc atctgtgtga ctgtgtgga  
361 cctctctcgg ggaggcatta tgtatattat ttccggatca ctctggcag caacggagaa  
421 aaactccagg aagtgtttgg tcaaaggaaa aatgataatg aattcattga gcctctttgc  
481 tgccatttct ggaatgatc ttcaatcat ggacatactt aatattaaaa ttccattt  
541 tttaaaaatg gagagtctga attttattag agctcacaca ccatatatta acatatacaa  
601 ctgtgaacca gctaaccct ctgagaaaaa ctcccatct acccaatact gttacagcat  
661 acaatctctg ttctgggca tttgtcagt gatctgac ttgccttct tccaggaact  
721 tgtaatagct ggcacgttg agaatgaatg gaaaagaacg tgcctcagac ccaaactcaa  
781 catagtctc ctgtcagcag aagaaaaaaa agaacagact attgaaataa aagaagaagt  
841 ggttgggcta actgaacat ctcccaacc aaagaatgaa gaagacattg aaattattcc  
901 aatccaagaa gaggaagaag aagaacaga gacgaactt ccagaacctc occaagatca  
961 ggaatcctca ccaatagaaa atgacagctc tccttaagt atttctctg tttctgtt  
1021 ccttttttaa acattagtgt tcatagcttc caagagacat gctgacttc atttctgag  
1081 gtactctgca catacgacc acatctctat ctggccttg catggagtga ccatagctcc  
1141 ttctctcta catgaatgt agagaatgta gccattgtag cagcttgtgt tgcacgctt  
1201 ctcttttga gcaactttct tacactgaag aaaggcagaa tgagtgttc agaattgat  
1261 ttctactaa cctgttcctt ggataggctt tttagtatag tattttttt ttgtcattt  
1321 ctccatcagc aaccaggag actgcacctg atggaaaaga tatatgactg ctcatgaca  
1381 ttctaaact atctttttt tattccacat ttattacgtttt ggtggagtc ctttgcac  
1441 attgttttaa ggatgataaa aaaaaaaaaa aaa

## FIGURE 23C

1 tgttaaacca aagtaattgg agcgaagccc agggtagcag aagctactga ttctctgtca  
61 cctgatgtct atcagcgatt tcatcttcag gcctggacta caccactcac cctcccagtg  
121 tgcttgagaa acaaactgca ccactgaac tccgcagcta gcatccaaat cagcccttga  
181 gatttgaggc ctggagact caggaagga atcaatttgc ttctttaa tgacttaaag  
241 gaggtgatgg ataaggata gaatggttt gaagactgga ggttctgat ctaattcta  
301 gagttccct agtcagact cctaatagtt ctatgactta aggaggggag acgatatcaa  
361 ggcttgctgc ccactcactc ctctaatacag tctccctctc aacaattacc ctatgcagtc  
421 aactgtgaat cattccacaa aagtagtaga ttgcagcata tataataaat catggtttct  
481 aaaccattgg gttcgaactg gagctctacc actaacaaac aatataacct tgggcaaatt  
541 actaacctct aagcctcagc ttctcatcg ttaacttatt tatgtcttac atctcagaga  
601 ggggtactgt tctaacttta cagaaggata aaatcgaaac taatgctcag caaagtacaa  
661 agaacaagaa tagcaacaaa aataactatt tattcaaca tgggttcttt gcatacatt  
721 atttcttcaa taatatttat taagaagtaa cttaatccaa aaattatttt agatcctgaa  
781 caagagagaa caaaatctct actttgatgg aacttccatt ctgtggggaa gagactgaca  
841 ataagcaatt aaataaataa ggtaatttcc tacagtgatc aatgccgtaa agcaattaag  
901 ataggatttt gtaaaagaca gcaaatagga gtacatgtta tagattgagg gttcaaggta  
961 ggctcctcta ggagctgaca ttgagctac acctgaacaa aaagacacta gccatgcaca  
1021 gaccatgagc ccagttaagt gttatagcag cccacgagat aagaattatt attatttcaa  
1081 ttctacagt gaacctgagg ccagagaaat ttaaagaact tgccaacat ctcagaacaa  
1141 atggaggaat cactattgaa acctgggcaa tctgactcag gaggccacag tcttatatac  
1201 tgacattaga aagccttaga gagccttttc ttttctttg agaccgagtc tcaactctgt  
1261 acccaggctg gaatgcagtg gcatgatctc agctcactgc aacctctgcc tcttaggttc  
1321 aagcaattct cctgccttag cctcccgagt agctgggatt acagggtcac accaactatg  
1381 ctggctaatt ttgtatttg tagtagagat ggggttttgc catgttagcc agcccggtct  
1441 caaacctctg acctcagggt atctgccc attggcctcc caaagtgtt ggattacagg  
1501 catgagccac cgtgcccagc ctgagagacc ttcttgatgt gactgcaca aggtggcaga  
1561 gttagagaca gagagaggcc tggaatcgac cctcctgct tctacagata gtccttacca  
1621 tactctgcaa tgtgcctct ggccatcata atgcacaaag gcagataagc aaaaggacaa  
1681 ggacaagtcc attgaaaata catttttcaa tattaagca aaagaaaagc atccaggaat  
1741 aagaaacaaa gaggacatgc agtcatatat gcaagggtgc ctctacaaag ataaagaatg  
1801 ccccaaacc agttgtcaag atcactggca gggactcctg ggcccacatg ctcttcttaa  
1861 acaacccctc catctccttt ctcagaactc agcagtaggc ctgacctcag atccaaggtc  
1921 actcggaaga ggccatgtct acctcaatg aactcatgg aggaaatgt gagagaagca  
1981 ttcagatgca tgacacaagg taagactgcc aaaaatcttg ttctgtctct cctcattttg  
2041 ttattgttt tatttttagg agtttgaga gcaaaatgac aacaccaga aattcagtaa

**FIGURE 23C**  
**(CONT'D)**

2101 atgggacttt cccggcagag ccaatgaaag gccctattgc tatgcaatct ggtccaaaac  
2161 cactcttcag gaggatgtct tcactggtgg gccccacgca aagcttcttc atgaggggaat  
2221 ctaagacttt gggggtaagt cagtgcctt ccatcccatg tcgtagggat tctctggctg  
2281 acagaagctg atgcggtata ggtcacatac agaattcaat ccaatttgaa gaattgggat  
2341 ccaacctgat gtctcttta tgtctaacac agtgggcaa atcaggggtg catcagagaa  
2401 gttatcactt agatcacctc tgggtgatct tatgtacct ttgggtttg gggctgtat  
2461 atgcaggggt tccccattc ccagttccat ttgccagaat cccaggcata cctgtctcct  
2521 ggaaatgccc catgtggttg aggaaacaga ttcgaacaag aaaaagacaa aattcttggc  
2581 acctccactg ctctcttag gcattcctca cagctccaag tcaggagcca gagcttcaa  
2641 cctgtcttt gccgtctagc agtgatgatt tcagctcct cactgtgcc tctgtctct  
2701 cccaggctg tccagattat gaatgggctc ttccacattg cccgtggggg tctctgatc  
2761 atyccagcag ggatctatgc acctatctgt gtgactgtgt ggtacctct ctggggaggc  
2821 attatggtga gtaaaagaat agcagccatt tgggaaatgg tgcagacaaa aatgttaaaa  
2881 ggctccacag ggatatgcca gattattct gtgttgaggg aaatatatga gtaggaaata  
2941 ttattgggtt aaagtaatta agaagacagg ttgaccaaat tgagtataaa tcccatggtt  
3001 gagagtcagt ggtcctgttt catgtgaatt cagagaaagg ggccctgcat ggatctcaca  
3061 gggactgtcc aaagcaagaa ctctccaaag tcagttctgg tggggagggt ggccctagac  
3121 atttagacta galagcaaga tgttttgaa agcaagaggc agcaggaaca tccactcca  
3181 tctaccctt ctgtctaca attctgttg gttactatgg tacctggtga aacctgtccc  
3241 atcacaagtc agtctcattt tgcttatoga cagagcagca ctctttgac gtttatgta  
3301 catgtttcc aaatctgtaa cctgtctgg gtgtgattg agttctgtct ctttggtctt  
3361 actatatcc tgcacagat cccagatga ttgagtaaaa ggcatgaatt tagtgtact  
3421 gagcctgaat aaaggaggaa tatgacagct gaaaaatgaa tacaactgat aaaaatgggt  
3481 ggaagggtgt gtgaaagtgt ctgaaagtgt aggcctctt ctgaccagtt atcaatgta  
3541 aaaagtatc tctctctcc tctatctct gtcttgccca cccctctcc atctcccca  
3601 cctctcttt ttacagtata ttattccgg atcactctg gcagcaacgg agaaaaactc  
3661 caggaagtgt ttggcaagta accatatgtc ctctttccc acatgtcaga gaagtaccta  
3721 ttttttcgg ttaaaaactg agaccctaa aaagccatgg tatcacagcc tctcagcct  
3781 aaaaagcaaa gacctccac aatgttatg tgattttatt tatgaaaaac ttagaagcga  
3841 gatcatctga agtatgttca tgggaacaga actaaaagca gatccatgaa aaccatacct  
3901 acagtctaa gaacgttaaa tgcgtgtga aaataataga ccttcngaa gccctatcat  
3961 ttctcccaga tcaccattta ggaaattatc tgatcaatgt catgatgat tcaaaattct  
4021 agctaagcca tttttggtc gtaacattga acaagtcagt ttaccttat gttoctgagt  
4081 ttacactgg aaaggaaggg taacagtctt tctaccatg tgacgtcaa tggagtgaag  
4141 gcagtagagt gtgtgatgt gcttcacagg actataggta ctacactgtg gtcttgccca  
4201 taaaaccctt ggggaactca tatagatcca gaggaaactg gctgcaggcg cgagcgaagg  
4261 gtgaaaagag tttagcagca agttcgctcc caaaaaattc ctcccccaac actgttacta

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## FIGURE 23C (CONT'D)

4321 aactgtgtca cttcataatc aatgagggaa tgggtggatt gagatgggtc ctgtcttaa  
4381 agtgacctga cacactcagt ttggggggaa aacttttat gaacatcaaa ttattctta  
4441 gatacagcca gatttactga ctgcatgt gtaggtcata gagctaggaa tgaaatatgc  
4501 gcaacataaa ataataatca ataatccat atcattatgg tactgttat ttatatttc  
4561 ctgttcaac ctttatcat cctgcaagg tagaacattc acactgatat tctcttacct  
4621 atgctacca aagacatcag ccctaattgt atttggaag atagctgact ggggctgatt  
4681 gcagcctatg tcagcaggaa tagatgtgt tactgtgtt gctctgctt ttttatttc  
4741 catttattg atagtacaga tctagagggt tctatctgaa ccttcccaac ctatactca  
4801 taataccatc ccactaaagt gtgatacaag aaactcttc actctcttc cctacatct  
4861 ttatgaaggc agataataaa ctggataata ttatcttca cttattcaac aaacatttat  
4921 tgagtgccta ctaggatggt ggcagtggca gtgaaggaaa tgcaaggata caagatatag  
4981 aatcaagggt tactcttaga attttgctt tataaaacag atggatgggt aatgagatag  
5041 ggaagactga gaaaacaaca ggatagagac atgatttat ttatagtga caaagaggct  
5101 aaaaagaact gagagaactt cagtatatat agttgtagt gcttgtgag tcagggcagt  
5161 tgcatttga attccctccc agattatgt ttccaaagg aaatcaaacc caattaataa  
5221 atctgtgct ccaattcagg tcaaaggaaa aatgataatg aattcatga gcctcttgc  
5281 tgccattct ggaatgattc ttcaatcat ggacatactt aatattaaaa ttccattt  
5341 ttataaatg gagagtctga atttattag agctcacaca ccatatatta acatatataa  
5401 ctgtgaacca gctaaccct ctgagaaaaa ctcccatct acccaatact gttacagcat  
5461 acaatctctg tcttggtaa gtgtcttg taagtgtgag attggattc tctccaggga  
5521 ggaaggatga ctgtttatt atgagcatga actctgaatt ccagaccacc tgtgttgc  
5581 tgcttcaact gattattcat acctacitt ctatcagcaa tacacattaa ccatctgtg  
5641 tgtgcaaaa gtgtgttaa gagttagggt tataaagatg ctgtctctg tactagcagt  
5701 tctcacagct attcattact tcttaaaga attgatctt taatcgttca attatagtca  
5761 acaataactt actgaacacc aacaatgttc ttgtgcat tattacattt tcaccttcat  
5821 tctctgtg ttttcaggg cattttgca gtgatgtga tcttgcctt ctccaggaa  
5881 ctgtaatag ctggcatcgt tgagaatgaa tggaaaagaa cgtgtccag acccaaatct  
5941 glaagtagta gccccagca ccgtggtaa tgtctgctgc cctgaagat ttattcagac  
6001 ttgagttta ataatgact tgataaggat ataagcacct gcaaaaaaat ttggcattt  
6061 aaaggcatat aataaatgac ataagtagca taaaaccag gaggtatttg ataatgttt  
6121 gtggagattg ttgacaaagg tgcagttgt aaaagtaaag aatggttgt ttaatttct  
6181 gttttagaac atagtctcc tgcagcaga agaaaaaaa gaacagacta ttgaaataaa  
6241 agaagaagt gtgggctaa ctgaaacatc ttccaacca aagaatgaag aagacattga  
6301 aattattcca atccaagaag aggaagaaga agaaacagag acgaacttc cagaacctcc  
6361 ccaagatcag gaatcctcac caatagaaaa tgacagctct ccttaa

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## FIGURE 23D

Mouse CD20

1 gaattccttt tttttttt ttttaaaga tttatttatt attatatgta agtacactgt.  
61 agctatcttc aagtacttga gatagaagag gccaaactgat ctacagctgtg agtggctaata  
121 ttggccctta agccttggag ccttggagccc ttggagacccc aggcgtttga aaactcaatg  
181 agtggacctt tcccagcaga gcctacaaaa ggtoctctcg ccatgcaacc tgciccaaaa  
241 gtgaacctca aaaggacatc ttcactgggtg ggccccacac aaagcttctt catgagggaa  
301 tcaaaggctt tgggggctgt ccaaatcatg aatggcctct tccatattac cctggggggga  
361 ctgctgatga tccccacagg ggtcttcgca cccatctgtt tgagtgtatg gtaccctctc  
421 tggggaggca ttatgtacat tatttcagga tcaactcctgg cagctgcagc agaaaaaac  
481 tccaggaaga gtttggtcaa agcaaaagt ataataagct ctctaagcct ctttgcctgc  
541 atttctggaa taattcttc aatcatggac atacttaaca tgacacttc tcaattttta  
601 aaaatgagaa gactggagct tattcaaact tccaagccgt atgttgatat ctacgactgt  
661 gaaccatcta attcctcaga gaaaaactcc ccatctacac agtactgtaa cagcattcag  
721 tctgtgtct tgggcattct gtggcgatg ctgatctctg ccttcttcca gaaactgtg  
781 acagctggta ttgtggagaa tgagtggaaa agaattgtga ccagatccaa atctaattg  
841 gtictgctgt cagctggaga aaaaaatgag cagacgatta aaatgaaaga agaaatcatt  
901 gagctaagtg gagtatcttc ccaaccaaag aatgaagagg aaattgaaat tattccagt  
961 caggaggaag aagaagaaga agcagaaata aattttccag cacctcccca agagcaggaa  
1021 tcttgccag tggaaaatga gatcgctct taaactctt tctttctaa gcattattgt  
1081 ttagagagct tccaagacac atagttaccc tcatctcttg tggccttcca caatctattc  
1141 tccatatttt cacagcttaa ctttgcatag agaagccaca tctagctctc cttcacattt  
1201 gaagaatgca gtgattataa aagattgtct ttgccttgc ttagggagtc ttacactggc  
1261 agaaacgctg aagaatcaa ttctcattca ccttttcctt ggaatgtgtg ctacagtagt  
1321 gtaatgggtt tccgcattt cctccatcag cagttacagc agaaggagtc agagagttca  
1381 gggaattc

FIGURE 24

Macrophages and natural killer cells express transgenic human CD16

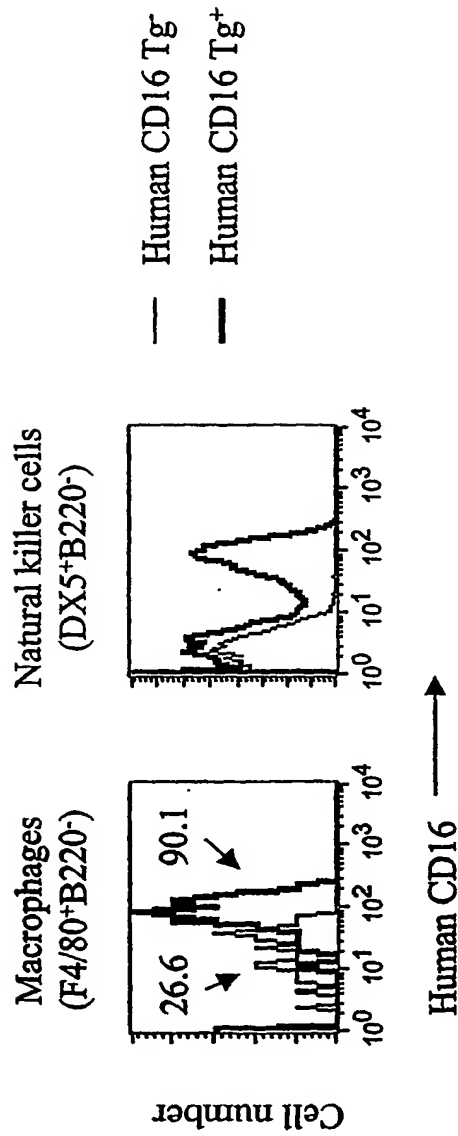


Figure 25A

Fc Receptor gamma Chain

1 mipavvllll llveqaaalg epqlcyilda ilflygivlt llycrkiquv rkaaitsyek  
61 sdgvvtglst rnqetyetlk hekppq

Figure 25B

1 cagaacggcc gatctccagc ccaagatgat tccagcagtg gtcttgctct tactcctttt  
61 ggtgaacaa gcagcggccc tgggagagcc tcagctctgc tatatcctgg atgccatcct  
121 gtttctgtat ggaattgtcc tcaccctcct ctactgtcga ctgaagatcc aagtgcgaaa  
181 ggcagctata accagctatg agaaatcaga tgggtgttac acgggcctga gcaccaggaa  
241 ccaggagact tacgagactc tgaagcatga gaaaccacca cagtagcttt agaatagatg  
301 cggatcatatt ctctttggc ttctggttct tccagccctc atggttgga tcacatatgc  
361 ctgcatgcca ttaacaccag ctggccctac ccctataatg atcctgtgtc cttaaattaat  
421 atacaccagt gggtcctcct ccctgttaaa gactaatgct cagatgctgt ttacggatat  
481 ttatattcta gtctcactct ctgtccac ccttctctc tccccattc ccaactccag  
541 ctaaaatatg ggaaggaga accccaata aaactgcat ggactggact c

10/537963

## FIGURE 26

### FACS staining of mouse CD16

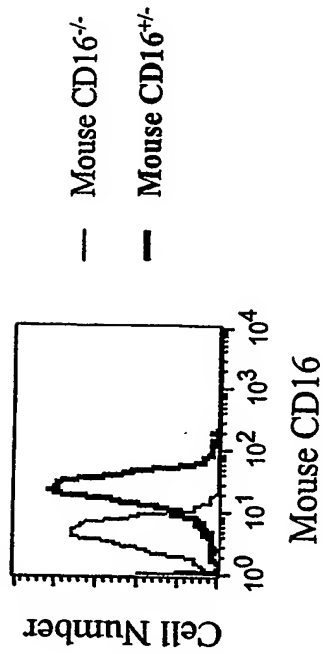




Figure 27

Expression of mouse CD64 in peripheral blood of CD16<sup>-/-</sup> mice

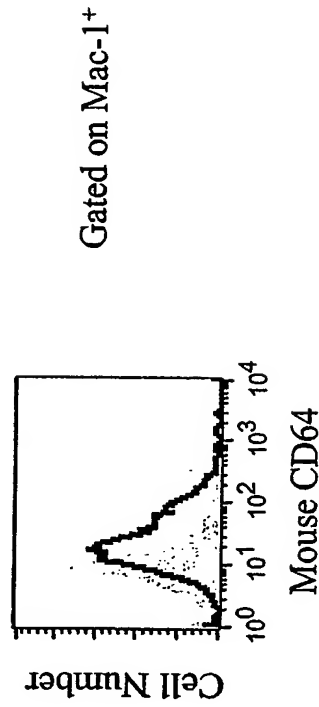
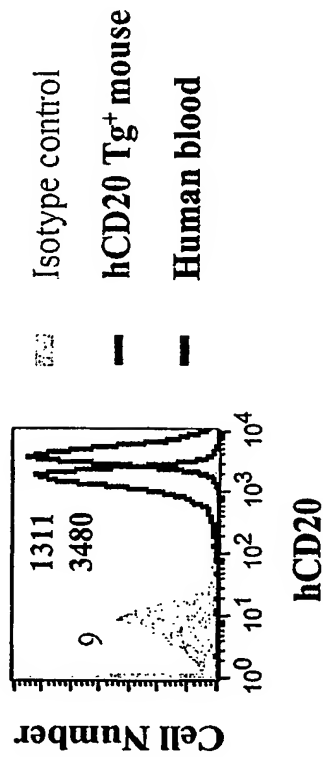


Figure 28

# Human CD20 expression in peripheral blood



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